

A first update on mapping the human genetic architecture of COVID-19

<https://doi.org/10.1038/s41586-022-04826-7>


COVID-19 Host Genetics Initiative*[✉]

Received: 4 November 2021

Accepted: 29 April 2022

Published online: 3 August 2022

Open access

 Check for updates

The COVID-19 pandemic continues to pose a major public health threat, especially in countries with low vaccination rates. To better understand the biological underpinnings of SARS-CoV-2 infection and COVID-19 severity, we formed the COVID-19 Host Genetics Initiative¹. Here we present a genome-wide association study meta-analysis of up to 125,584 cases and over 2.5 million control individuals across 60 studies from 25 countries, adding 11 genome-wide significant loci compared with those previously identified². Genes at new loci, including *SFTPD*, *MUC5B* and *ACE2*, reveal compelling insights regarding disease susceptibility and severity.

Here we present meta-analyses bringing together 60 studies from 25 countries (Fig. 1 and Supplementary Table 1) for three COVID-19-related phenotypes: (1) individuals critically ill with COVID-19 on the basis of requiring respiratory support in hospital or who died as a consequence of the disease (9,376 cases, of which 3,197 are new in this data release, and 1,776,645 control individuals); (2) individuals with moderate or severe COVID-19 defined as those hospitalized due to symptoms associated with the infection (25,027 cases, 11,386 new and 2,836,272 control individuals); and (3) all cases with reported SARS-CoV-2 infection regardless of symptoms (125,584 cases, 76,022 new and 2,575,347 control individuals). Most studies have reported results before the roll out of the COVID-19 vaccination campaign. An overview of the study design is provided in Supplementary Fig. 1. We found a total of 23 genome-wide significant loci ($P < 5 \times 10^{-8}$) of which 20 loci remain significant after correction for multiple testing ($P < 1.67 \times 10^{-8}$) to account for the number of phenotypes examined (Fig. 2, Supplementary Fig. 2 and Supplementary Table 2). We compared the effects of these loci between the previous² and current analysis and found that only one locus did not replicate (rs72711165). All of the other loci showed the expected increase in statistical significance (Supplementary Fig. 3).

Across the genome-wide significant loci, we observed clear patterns of association with the different phenotypes under study. We therefore developed a two-class Bayesian model for classifying loci based on the patterns of association across the two better-powered phenotypes (COVID-19 hospitalization and SARS-CoV-2 reported infection). Intuitively, loci that are associated with susceptibility will also be associated with severity as, to develop COVID-19, SARS-CoV-2 infection needs to first occur. By contrast, those genetic effects that solely modify the course of illness should be associated with severity of illness and not show any association with reported infection except through preferential ascertainment of hospitalized cases in a cohort (Supplementary Methods). We identified 16 loci that are substantially more likely (>99% posterior probability) to affect the risk of COVID-19 hospitalization

and 7 loci that clearly influence susceptibility to SARS-CoV-2 infection (Supplementary Table 3 and Supplementary Fig. 4).

We observed that several loci had a significant heterogeneous effect across studies (6 out of 23 loci with a P value for heterogeneity of $< 2.2 \times 10^{-3}$; Supplementary Table 2). Owing to an increased diversity in our study population (Supplementary Fig. 5), we were able to examine whether such heterogeneity was due to effect differences across continental ancestry groups. Only one locus (*FOXP4*) showed a significantly different effect across ancestries (P value heterogeneity of $< 7 \times 10^{-5}$; Supplementary Table 4 and Supplementary Fig. 6), although even at this locus all of the ancestry groups showed a positive effect estimate. This confirms that factors related to between-study heterogeneity (such as variable definition of COVID-19 severity owing to different thresholds for testing, hospitalization and patient recruitment) rather than differences across ancestries are a more likely explanation for the observed heterogeneity in the effect sizes across studies.

For the 23 genome-wide significant loci, we examined candidate causal genes and performed a phenome-wide association study to better understand their potential biological mechanisms (Supplementary Tables 2, 5 and 6 and Supplementary Fig. 7). Several of these loci with previous and direct connections to lung disease and SARS-CoV-2 infection mechanisms are highlighted here.

Several loci involved in COVID-19 severity implicate lung surfactant biology. A missense variant rs721917:A>G (p.Met31Thr) in *SFTPD* (10q22.3) confers risk for hospitalization (odds ratio (OR) = 1.06, 95% confidence interval (CI) = 1.04–1.08, $P = 1.7 \times 10^{-8}$) and has been previously associated with increased risk of chronic obstructive pulmonary disease³ (OR = 1.08, $P = 2.0 \times 10^{-8}$) and decreased lung function⁴ ($FEV_1/FVC; \beta = -0.019; P = 2.0 \times 10^{-15}$). *SFTPD* encodes surfactant protein D (SP-D), which participates in innate immune response, protecting the lungs against inhaled microorganisms. The recombinant fragment of SP-D binds to the S1 spike protein of SARS-CoV-2 and potentially inhibits binding to ACE2 receptor and SARS-CoV-2 infection⁵. Another missense variant rs117169628:G>A (p.Pro256Leu) in *SLC22A31* (16q24.3) also confers risk of hospitalization (OR = 1.09, 95% CI = 1.06–1.13, $P = 2.6 \times 10^{-8}$). *SLC22A31* belongs to the family of solute carrier proteins that facilitate transport across membranes⁶ and is co-regulated with other surfactant proteins⁷.

We found that the variant rs35705950:G>T located in the promoter of *MUC5B* (11p15.5) is protective against hospitalization (OR = 0.83, 95% CI = 0.86–0.93, $P = 6.5 \times 10^{-9}$). This well-studied promoter variant increases the expression of *MUC5B* in lung in GTEx ($P = 6.7 \times 10^{-16}$) and is the strongest known variant associated with an increased risk of

*A list of authors and their affiliations appears at the end of the paper. ✉e-mail: aganna@broadinstitute.org

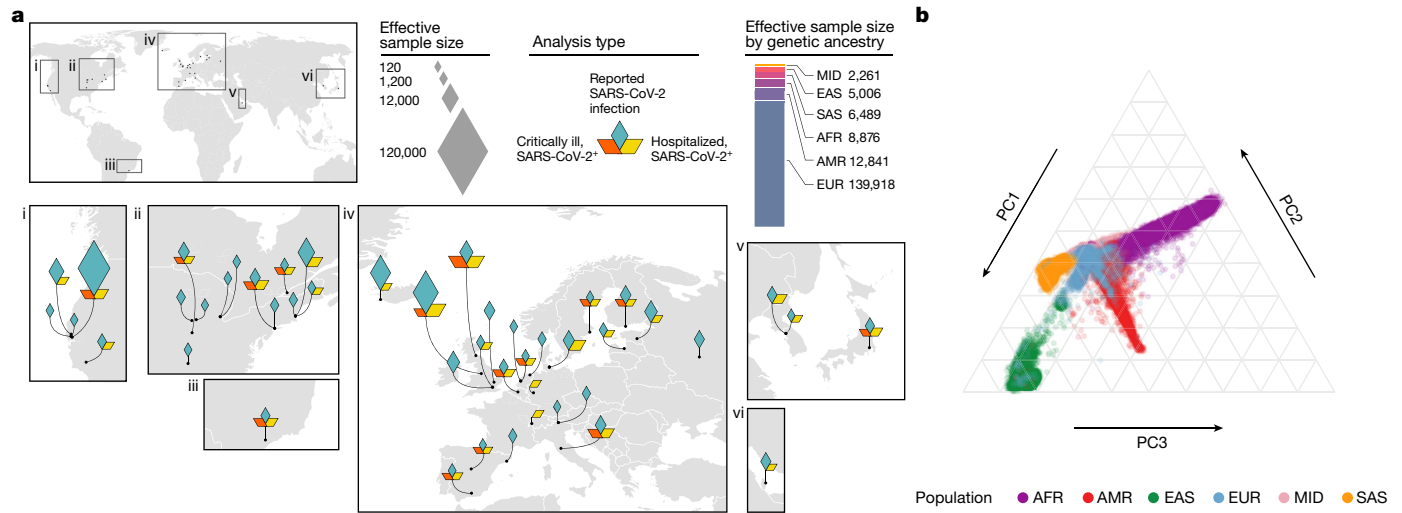


Fig. 1 | Overview of contributing studies in Host Genetics Initiative data freeze 6. **a**, Geographical overview of the contributing studies to the COVID-19 Host Genetics Initiative and composition by major continental ancestry groups. Ancestry groups are defined as Middle Eastern (MID), south Asian (SAS), east Asian (EAS), African (AFR), admixed American (AMR) and European (EUR). **b**, Principal components analysis highlighting the population structure and the sample ancestry of the individuals participating in the COVID-19 Host Genetics Initiative. This figure is reproduced from the original publication by the COVID-19 Host Genetics Initiative² with modifications reflecting the updated analysis from data freeze 6.

developing idiopathic pulmonary fibrosis (IPF)^{8,9}, but also improves survival in patients with IPF carrying this mutation¹⁰.

Finally, we found that rs190509934:T>C, which is located 69 bp upstream of *ACE2* (Xp22.2), is associated with decreased susceptibility risk (OR = 0.69, 95% CI = 0.63–0.75, $P = 3.6 \times 10^{-18}$). *ACE2* is the SARS-CoV-2 receptor and functionally interacts with *SLC6A19* and

*SLC6A20*¹¹, one of which also showed a significant association with susceptibility (rs73062389:G>A at *SLC6A20*; OR = 1.18, 95% CI = 1.16–1.20, $P = 2.5 \times 10^{-74}$). Notably, rs190509934 is ten times more common in south Asian populations (minor allele frequency (MAF) = 0.027) than in European populations (MAF = 0.0024), demonstrating the importance of diversity for variant discovery. Recent results have shown that the

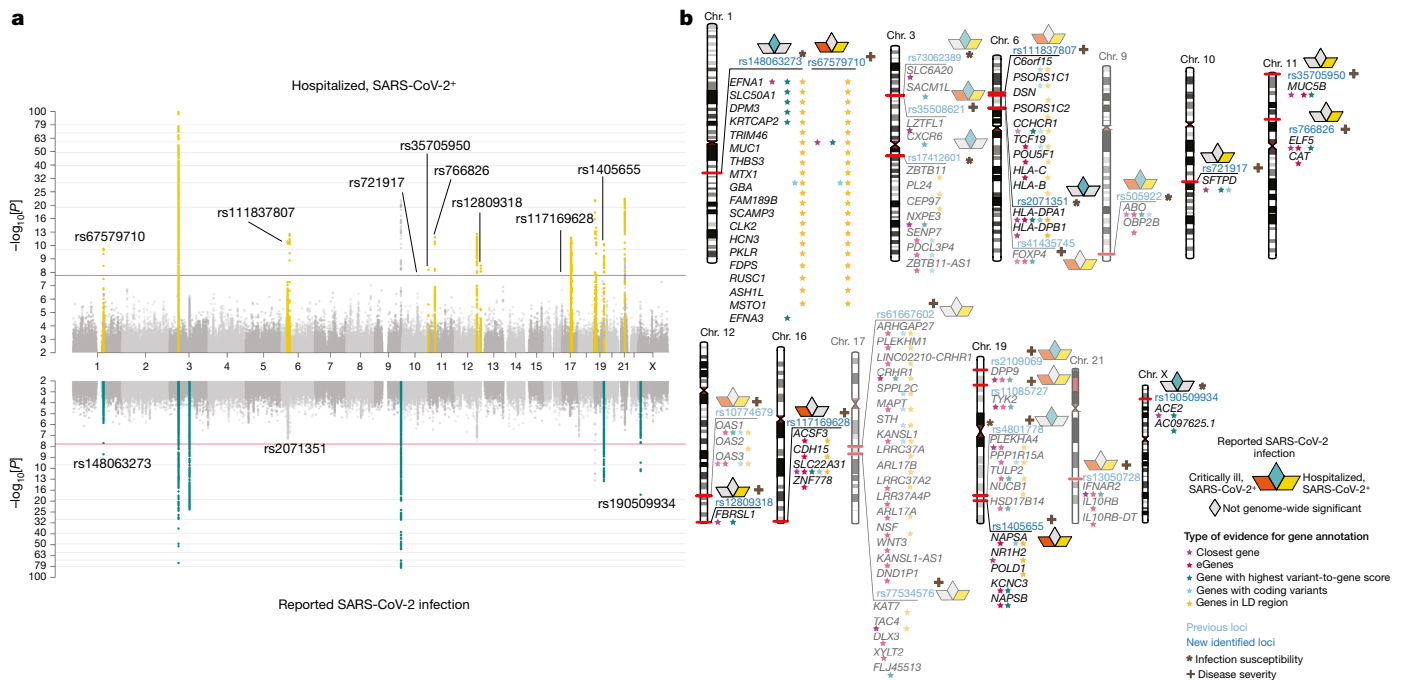


Fig. 2 | Genome-wide association results for COVID-19. **a**, The results of the genome-wide association study of hospitalized COVID-19 ($n = 25,027$ cases and $n = 2,836,272$ control individuals) (top), and the results of reported SARS-CoV-2 infection ($n = 125,584$ cases and $n = 2,575,347$ control individuals) (bottom). Loci highlighted in yellow (top) represent regions associated with the severity of COVID-19 manifestation. Loci highlighted in green (bottom) are regions associated with SARS-CoV-2-reported infection. Lead variants for the loci identified in this data release are annotated with their respective rs ID. Horizontal lines denote genome-wide significant thresholds. **b**, The results of gene prioritization using different evidence measures of gene annotation.

Genes in regions of linkage disequilibrium (LD), genes with coding variants and eGenes (fine-mapped *cis*-eQTL variant $PIP > 0.1$ in GTEx Lung) are annotated if in linkage disequilibrium with a COVID-19 lead variant ($r^2 > 0.6$). V2G denotes the highest gene prioritized by OpenTargetGenetics' V2G score. The asterisk (*) indicates SARS-CoV-2 reported infection and the plus symbol (+) indicates COVID-19 severity. The transparent loci were reported in the previous freeze (data release 5), and loci in bright blue were identified in the current freeze (data release 6). This figure is reproduced from the original publication by the COVID-19 Host Genetics Initiative² with modifications reflecting the updated analysis from data freeze 6.

rs190509934:T>C variant lowers *ACE2* expression, which in turn confers protection against SARS-CoV-2 infection¹².

We applied Mendelian randomization to infer potential causal relationships between COVID-19-related phenotypes and their genetically correlated traits (Supplementary Methods; Supplementary Tables 7–9 and Supplementary Fig. 8). A causal association was observed between genetic liability to type 2 diabetes and SARS-CoV-2 reported infection (OR = 1.02, 95% CI = 1.01–1.03, $P = 1.6 \times 10^{-3}$), and COVID-19 hospitalization (OR = 1.06, 95% CI = 1.03–1.1, $P = 1.4 \times 10^{-4}$). Multivariable Mendelian randomization was used to estimate the direct effect of liability to type 2 diabetes on COVID-19-related phenotypes that was not mediated through body mass index. This analysis indicated that the observed causal association of liability to type 2 diabetes on COVID-19 phenotypes is mediated by body mass index (Supplementary Table 10).

We have substantially expanded the genetic analysis of SARS-CoV-2 infection and COVID-19 severity by doubling the case size, identifying 11 loci. We developed an approach to systematically assign the 23 discovered loci to either disease susceptibility (7 loci) or disease severity (16 loci). Although distinguishing between the two phenotypes is challenging because progression to a severe form of the disease requires susceptibility to infection in the first place, it is now evident that the genetic mechanisms involved in these two aspects of the disease can be differentiated. Among the new loci associated with disease susceptibility, *ACE2* represents an expected, albeit interesting, finding. *MUC5B*, *SFTPD* and *SLC22A31* are the three most interesting new loci associated with COVID-19 severity. Their relationship with lung function and lung diseases is consistent with loci previously associated with disease severity. The surfactant proteins secreted by alveolar cells, representing an emerging biological mechanism, maintain healthy lung function and facilitate the clearance of pathogens¹³. The protective effect of the *MUC5B* variant is unexpected given the otherwise risk-increasing, concordant effect between IPF and COVID-19 observed for other variants⁹. Nonetheless, this result aligns with the *MUC5B* promoter variant association that shows a twofold higher survival rate among patients with IPF¹⁰. In mice, *Muc5b* seems to be essential for effective mucociliary clearance and for controlling infection¹⁴, which suggests that therapies to control mucin secretion may be beneficial in patients with COVID-19.

Expanding genomic research to include participants from around the world enabled us to test whether the effect of COVID-19-related genetic variants was markedly different across ancestry groups. We did not detect obvious heterogeneity between ancestry groups, and we attribute the observed heterogeneity in the effect of COVID-19-related genetic variants to the diverse inclusion criteria across studies in terms of COVID-19 severity. However, we also note that ascertainment differences across studies might mask true underlying differences in effect sizes between ancestry groups.

The biological insights gained by this expansion of the COVID-19 Host Genetic Initiative showed that increasing sample size and diversity remain a fruitful activity to better understand the human genetic architecture of COVID-19.

Reporting summary

Further information on research design is available in the Nature Research Reporting Summary linked to this paper.

Online content

Any methods, additional references, Nature Research reporting summaries, source data, extended data, supplementary information, acknowledgements, peer review information; details of author contributions and competing interests; and statements of data and code availability are available at <https://doi.org/10.1038/s41586-022-04826-7>.

Data availability

Summary statistics generated by COVID-19 Host Genetics Initiative are available online (<https://www.covid19hg.org/results/r6/>). The analyses described here use the freeze 6 data. The COVID-19 Host Genetics Initiative continues to regularly release new data freezes. Summary statistics for samples from individuals of non-European ancestry are not currently available owing to the small individual sample sizes of these groups, but the results for 23 loci lead variants are reported in Supplementary Table 3. Individual-level data can be requested directly from the authors of the contributing studies, listed in Supplementary Table 1. We used publicly available data from GTEx (<https://gtexportal.org/home/>), the Neale laboratory (<http://www.nealelab.is/uk-biobank/>), the Finucane laboratory (<https://www.finucanelab.org>), the FinnGen Freeze 4 cohort (https://www.finnngen.fi/en/access_results) and eQTL catalogue release 3 (<http://www.ebi.ac.uk/eqtl/>).

Code availability

The code for summary statistics lift-over, the projection PCA pipeline including precomputed loadings and meta-analyses are available on GitHub (<https://github.com/covid19-hg/>), and the code for the Mendelian randomization and genetic correlation pipeline is available at GitHub (<https://github.com/marcoralab/MRcovid>). Codes for implementing the multivariable Mendelian randomization analysis and subtype analyses are available at GitHub (https://github.com/marcoralab/multivariate_MR) and https://github.com/mjpirinen/covid19-hgi_subtypes).

1. The COVID-19 Host Genetics Initiative. The COVID-19 Host Genetics Initiative, a global initiative to elucidate the role of host genetic factors in susceptibility and severity of the SARS-CoV-2 virus pandemic. *Eu. J. Hum. Genet.* **28**, 715–718 (2020).
2. COVID-19 Host Genetics Initiative. Mapping the human genetic architecture of COVID-19. *Nature* **600**, 472–477 (2021).
3. Hobbs, B. D. et al. Genetic loci associated with chronic obstructive pulmonary disease overlap with loci for lung function and pulmonary fibrosis. *Nat. Genet.* **49**, 426–432 (2017).
4. Shrine, N. et al. New genetic signals for lung function highlight pathways and chronic obstructive pulmonary disease associations across multiple ancestries. *Nat. Genet.* **51**, 481–493 (2019).
5. Hsieh, M.-H. et al. Human surfactant protein D binds spike protein and acts as an entry inhibitor of SARS-CoV-2 pseudotyped viral particles. *Front. Immunol.* **12**, 641360 (2021).
6. Hediger, M. A. et al. The ABCs of solute carriers: physiological, pathological and therapeutic implications of human membrane transport proteins. *Pflugers Arch.* **447**, 465–468 (2004).
7. Deelen, P. et al. Improving the diagnostic yield of exome-sequencing by predicting gene-phenotype associations using large-scale gene expression analysis. *Nat. Commun.* **10**, 2837 (2019).
8. Seibold, M. A. et al. A common *MUC5B* promoter polymorphism and pulmonary fibrosis. *N. Engl. J. Med.* **364**, 1503–1512 (2011).
9. Fadista, J. et al. Shared genetic etiology between idiopathic pulmonary fibrosis and COVID-19 severity. *EBioMedicine* **65**, 103277 (2021).
10. Peljto, A. L. et al. Association between the *MUC5B* promoter polymorphism and survival in patients with idiopathic pulmonary fibrosis. *JAMA* **309**, 2232–2239 (2013).
11. Vuille-Dit-Bille, R. N. et al. Human intestine luminal *ACE2* and amino acid transporter expression increased by ACE-inhibitors. *Amino Acids* **47**, 693–705 (2014).
12. Horowitz, J. E. et al. Common genetic variants identify targets for COVID-19 and individuals at high risk of severe disease. Preprint at *medRxiv* <https://doi.org/10.1101/2020.12.14.20248176> (2021).
13. Wright, J. R. Immunoregulatory functions of surfactant proteins. *Nat. Rev. Immunol.* **5**, 58–68 (2005).
14. Roy, M. G. et al. *Muc5b* is required for airway defence. *Nature* **505**, 412–416 (2014).

Author contributions Detailed author contributions are integrated in the authorship list.

Competing interests A full list of competing interests is supplied as Supplementary Table 11.

Additional information

Supplementary information The online version contains supplementary material available at <https://doi.org/10.1038/s41586-022-04826-7>.

Correspondence and requests for materials should be addressed to Andrea Ganna.

Reprints and permissions information is available at <http://www.nature.com/reprints>.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Matters arising



Open Access This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons license, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons license and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this license, visit <http://creativecommons.org/licenses/by/4.0/>.

© The Author(s) 2022

COVID-19 Host Genetics Initiative Leadership

Gita A. Pathak¹, Juha Karjalainen², Christine Stevens³, Benjamin M. Neale⁴, Mark Daly^{2,3,5} & Andrea Ganna^{2,3,5,8,9}

Writing group

Writing group lead Gita A. Pathak¹, Shea J. Andrews⁶, Masahiro Kanai³, Mattia Cordioli⁷ & Andrea Ganna^{2,3,5}

Analysis group

Manuscript analyses team lead Juha Karjalainen²

Manuscript analyses team members: PHEWAS Gita A. Pathak¹ & Renato Polimanti¹

Manuscript analyses team members: Mendelian randomization Shea J. Andrews⁶ & Nadia Harerimana⁸

Manuscript analyses team members: methods development Mattia Cordioli⁷ & Matti Pirinen⁷

Manuscript analyses team members: PC projection, gene prioritization Masahiro Kanai³

Project management group

Project management lead Christine Stevens³ & Rachel G. Liao³

Project management support Karolina Chwialkowska⁹, Amy Trankiem³ & Mary K. Balaconis³

Website development

Huy Nguyen³ & Matthew Solomonson³

Scientific communication group

Scientific communication lead Kumar Veerapen³ & Brooke Wolford¹⁰

AncestryDNA COVID-19 Research Study

Analysis Team Lead Genevieve Roberts¹¹

Data collection lead Danny Park¹¹

Admin team lead Catherine A. Ball¹¹

Analysis team member Marie Coignet¹¹, Shannon McCurdy¹¹, Spencer Knight¹¹, Raghavendran Partha¹¹ & Brooke Rhead¹¹

Data collection member Miao Zhang¹¹, Nathan Berkowitz¹¹, Michael Gaddis¹¹, Keith Noto¹¹, Luong Ruiz¹¹ & Milos Pavlovic¹¹

Admin team member Eurie L. Hong¹¹, Kristin Rand¹¹, Ahna Girshick¹¹, Harendra Guturu¹¹ & Asher Haug Baltzell¹¹

BelCovid

Analysis team lead Mari E. K. Niemi¹²

Data collection lead Souad Rahmouni¹³ & Julien Guntz¹⁴

Admin team lead Yves Beguin¹⁵

Analysis team member Mattia Cordioli¹⁶, Sara Pigazzini¹² & Lindokuhle Nkambule^{17,18,19}

Data collection member Michel Georges¹³, Michel Moutschen^{20,21}, Benoit Misset^{20,21}, Gilles Darcis^{20,21}, Julien Guiot^{20,21}, Samira Azarzar^{20,21}, Stéphanie Gofflot¹⁵, Sabine Claassen¹⁴, Olivier Malaise²⁰, Pascale Huynen²⁰, Christelle Meuris²⁰, Marie Thys²⁰, Jessica Jacques²⁰, Philippe Léonard²⁰, Frederic Fripiat²⁰, Jean-Baptiste Giot²⁰, Anne-Sophie Sauvage²⁰, Christian Von Frenckell²⁰, Yasmine Belhaj¹³ & Bernard Lambertmont²⁰

Biobanque Quebec COVID-19

Analysis team lead Tomoko Nakanishi^{22,23,24,25}

Data collection lead David R. Morrison²³

Admin team lead Vincent Mooser²⁶ & J. Brent Richards^{23,27,28}

Analysis team member Guillaume Butler-Laporte^{23,29}, Vincenzo Forgetta²³ & Rui Li²⁶

Data collection member Biswarup Ghosh²³, Laetitia Laurent²³, Alexandre Belisle²⁶, Danielle Henry²³, Tala Abdullah²³, Olumide Adeleye²³, Noor Mamlouk²³, Nofar Kimchi²³, Zaman Afrasiabi²³, Nardin Rezk²³, Branka Vulesevic²³, Meriem Bouab²³, Charlotte Guzman²³, Louis Petitjean²³, Chris Tselios²³, Xiaoping Xue²³, Jonathan Afilalo²³, Marc Afilalo^{30,31}, Maureen Oliveira³², Bluma Brenner³³, Nathalie Brassard³⁴ & Madeleine Durand^{35,36}

Admin team member Erwin Schurr³⁷, Pierre Lepage²⁶, Jiannis Ragoussis³⁶, Daniel Auld²⁶, Michaël Chasse^{36,38}, Daniel E. Kaufmann^{36,39}, G. Mark Lathrop²⁶ & Darin Adra²³

CCHC COVID-19 GAWS

Analysis team lead Caroline Hayward⁴⁰, Joseph T. Glessner^{41,42} & Douglas M. Shaw⁴³

Data collection lead Archie Campbell^{44,45} & Marcela Morris⁴⁶

Admin team lead Hakon Hakonarson^{41,42}, David J. Porteous⁴⁴ & Jennifer Below⁴³

Analysis team member Anne Richmond⁴⁰, Xiao Chang⁴¹, Hannah Polikowski⁴³, Petty E. Lauren⁴³, Hung-Hsin Chen⁴³ & Zhu Wanying⁴³

Data collection member Chloe Fawns-Ritchie^{44,47}

Admin team member Kari North⁴⁸ & Joseph B. McCormick⁴⁶

CHOP CAG

Data collection member Xiao Chang⁴⁹, Joseph R. Glessner^{49,50} & Hakon Hakonarson^{49,51,52}

The Colorado Center for Personalized Medicine

Analysis team lead Christopher R. Gignoux⁵³

Data collection lead Stephen J. Wicks⁵³ & Kristy Crooks⁵³

Admin team lead Kathleen C. Barnes⁵³

Analysis team member Michelle Daya⁵³, Jonathan Shortt⁵³, Nicholas Rafaels⁵³ & Sameer Chavan⁵³

Coronagenes

Analysis team lead Paul R. H. J. Timmers^{54,55}, James F. Wilson^{54,55} & Albert Tenesa^{54,56}

Admin team lead Shona M. Kerr⁵⁴

Analysis team member Kenton D'Mellow⁵⁶

Egypt hgCOVID hub

Analysis team lead Mari E. K. Niemi¹²

Data collection lead Doaa Shahin⁵⁷ & Yasser M. El-Sherbiny^{57,58}

Admin team lead Kathrin Aprile von Hohenstaufen⁵⁹, Ali Sobh⁶⁰ & Madonna M. Eltoukhy⁶¹

Analysis team member Mattia Cordioli⁷ & Lindokuhle Nkambule^{17,62}

Data collection member Tamer A. Elhadidy⁶³, Mohamed S. Abd Elghafar⁶⁴, Jehan J. El-Jawhari^{67,58}, Attia A. S. Mohamed⁶¹, Marwa H. Elnagdy⁶⁵, Amr Samir⁶⁶, Mahmoud Abdel-Aziz⁶⁷, Walid T. Khafaga⁶⁸, Walaa M. El-Lawaty⁶⁹, Mohamed S. Torky⁶⁹ & Mohamed R. El-shanshory⁷⁰

Admin team member Amr M. Yassen⁷¹, Mohamed A. F. Hegazy⁶⁶, Kamal Okasha⁷², Mohammed A. Eid⁷³ & Hanteera S. Moahmed⁶⁹

EraCORE

Analysis team lead Carolina Medina-Gomez⁷⁴

Data collection lead M. Arfan Ikram⁷⁵

Admin team lead Andre G. Uitterlinden^{74,75}

Estonian Biobank

Analysis team lead Reedik Mägi⁷⁶

Data collection lead Lili Milani⁷⁶

Admin team lead Andres Metspalu⁷⁶

Analysis team member Triin Laisk⁷⁶, Kristi Läll⁷⁶ & Maarja Lepamets⁷⁶

Data collection member Tõnu Esko⁷⁶, Ene Reimann⁷⁶, Paul Naaber⁷⁷, Edward Laane^{78,79}, Jaana Pesukova⁷⁸, Pärt Peterson⁸⁰, Kai Kisand⁸⁰, Jekaterina Tabri⁸¹, Raili Allos⁸¹, Kati Hensen⁸¹, Joel Starkopf⁸², Inge Ringmets⁸³, Anu Tamm⁸⁴ & Anne Kallaste⁸⁴

Admin team member Helene Alavere⁷⁶, Kristjan Metsalu⁷⁶ & Mairo Puusepp⁷⁶

EXCEED

Analysis team lead Chiara Batini⁸⁵

Data collection lead Martin D. Tobin^{85,86}

Admin team lead Laura D. Venn⁸⁵

Analysis team member Paul H. Lee⁸⁵, Nick Shrine⁸⁵ & Alexander T. Williams⁸⁵

Data collection member Anna L. Guyatt⁸⁵, Catherine John⁸⁵, Richard J. Packer⁸⁵, Altaf Ali⁸⁵, Robert C. Free⁸⁷, Xueyang Wang⁸⁵, Louise V. Wain^{85,86} & Edward J. Hollox⁸⁸

Admin team member Catherine E. Bee⁸⁵ & Emma L. Adams⁸⁵

FinnGen

Aarno Palotie⁸⁹

Analysis team member Samuli Ripatti^{3,90,91} & Sanni Ruotsalainen⁹⁰

Data collection member Kati Kristiansson⁹², Sami Koskelainen⁹², Markus Perola^{92,93}, Kati Donner⁷, Katja Kivinen⁷ & Aarno Palotie⁷

Admin team member Mari Kaunisto⁷

Functional Host Genomics in Infectious Diseases (FHoGID)

Analysis team lead Carlo Rivolta^{94,95}

Data collection lead Pierre-Yves Bochud⁹⁶, Stéphanie Bibert⁹⁷, Noémie Boillat⁹⁶, Semira Gonseth Nussle⁹⁸ & Werner Albrich⁹⁹

Analysis team member Mathieu Quinodoz^{94,95} & Dhryata Kamdar^{94,95}

Data collection member Noémie Suh¹⁰⁰, Dionysios Neofytos¹⁰¹, Véronique Erard¹⁰² & Cathy Voide¹⁰³

FHoGID Pierre-Yves Bochud¹⁰⁴, Carlo Rivolta¹⁰⁴, Stéphanie Bibert¹⁰⁴, Mathieu Quinodoz¹⁰⁴, Dhryata Kamdar¹⁰⁴, Dionysios Neofytos¹⁰⁴, Véronique Erard¹⁰⁴, Cathy Voide¹⁰⁴, R. Friolet¹⁰⁴, P. Vollenweider¹⁰⁴, J. L. Pagani¹⁰⁴, M. Oddo¹⁰⁴, F. Meyer zu Bentrup¹⁰⁴, A. Conen¹⁰⁴, O. Clerc¹⁰⁴, O. Marchetti¹⁰⁴, A. Guillet¹⁰⁴, C. Guyat-Jacques¹⁰⁴, S. Foucras¹⁰⁴, M. Rime¹⁰⁴, J. Chassot¹⁰⁴, M. Jaquet¹⁰⁴, R. Merlet Viollet¹⁰⁴, Y. Lannepoudenc¹⁰⁴ & L. Portopena¹⁰⁴

RegCOVID P. Y. Bochud¹⁰⁵, P. Vollenweider¹⁰⁵, J. L. Pagani¹⁰⁵, F. Desgranges¹⁰⁵, P. Filippidis¹⁰⁵, B. Guéry¹⁰⁵, D. Haefliger¹⁰⁵, E. E. Kampouri¹⁰⁵, O. Manuel¹⁰⁵, A. Munting¹⁰⁵, M. Papadimitriou-Oliveris¹⁰⁵, J. Regina¹⁰⁵, L. Rochat-Stettler¹⁰⁵, V. Suttels¹⁰⁵, E. Tadini¹⁰⁵, J. Tschopp¹⁰⁵, M. Van Singer¹⁰⁵ & B. Viala¹⁰⁵

P-PredictUs N. Boillat-Blanco¹⁰⁶, T. Brahier¹⁰⁶, O. Hügli¹⁰⁶, J. Y. Meuwly¹⁰⁶ & O. Pantet¹⁰⁶

SeroCOVID S. Gonseth Nussle¹⁰⁷, M. Bochud¹⁰⁷, V. D'Acremont¹⁰⁷ & S. Estoppey Younes¹⁰⁷

CRIPSI W. C. Albrich¹⁰⁸, N. Suh¹⁰⁸, A. Cerny¹⁰⁸, L. O'Mahony¹⁰⁸, C. von Mering¹⁰⁸, P. Y. Bochud¹⁰⁸, M. Frischknecht¹⁰⁸, G-R. Kleger¹⁰⁸, M. Filipovic¹⁰⁸, C. R. Kahlert¹⁰⁸, H. Wozniak¹⁰⁸, T. Rochat Negro¹⁰⁸, J. Pugin¹⁰⁸, K. Bouras¹⁰⁸, C. Knapp¹⁰⁸, T. Egger¹⁰⁸, A. Perret¹⁰⁸, P. Montillier¹⁰⁸, C. di Bartolomeo¹⁰⁸ & B. Barda¹⁰⁸

GCAT Genomes For Life

Analysis team lead Rafael de Cid¹⁰⁹

Data collection lead Anna Carreras¹⁰⁹, Victor Moreno¹¹⁰ & Manolis Kogevinas^{111,112,113,114}

Analysis team member Iván Galván-Femenía¹⁰⁹, Natalia Blay¹⁰⁹, Xavier Farré¹⁰⁹ & Lauro Sumoy¹⁰⁹

Data collection member Beatriz Cortés¹⁰⁹, Josep Maria Mercader^{115,116,117,278}, Marta Guindo-Martinez¹¹⁸, David Torrents¹¹⁸, Judith Garcia-Aymerich^{111,113,114}, Gemma Castaño-Vinyals^{111,112,113,114} & Carlota Dobaño^{111,114}

GEN-COVID Multicenter Study

Analysis team lead Marco Gori^{119,120} & Mari E. K. Niemi¹²

Data collection lead Alessandra Renier^{121,122,123}, Francesca Mari^{121,122,123}, Mario Umberto Mondelli^{124,125}, Francesco Castelli¹²⁶, Massimo Vaghi¹²⁷, Stefano Rusconi^{128,129}, Francesca Montagnani^{130,131}, Elena Bargagli¹³¹, Federico Franchi¹³², Maria Antonietta Mazzei¹³³, Luca Cantarini¹³⁴, Danilo Tacconi¹³⁵, Marco Feri¹³⁶, Raffaele Scala¹³⁷, Genni Spargi¹³⁸, Cesira Nencioni¹³⁹, Maria Bandini¹⁴⁰, Gian Piero Caldarelli¹⁴¹, Anna Canaccini¹⁴², Agostino Ognibene¹⁴³, Antonella D'Armino Monforte¹⁴⁴, Massimo Girardis¹⁴⁵, Andrea Antinori¹⁴⁶, Daniela Francisci^{147,148}, Elisabetta Schiaroli^{147,148}, Pier Giorgio Scotton¹⁴⁹, Sandro Panese¹⁵⁰, Renzo Scaggiante¹⁵¹, Matteo Della Monica¹⁵², Mario Capasso^{153,154,155}, Giuseppe Fiorentino¹⁵⁶, Marco Castori¹⁵⁷, Filippo Aucella¹⁵⁸, Antonio Di Biagio¹⁵⁹, Luca Masucci^{160,161}, Serafina Valente¹⁶², Marco Mandalà¹⁶³, Patrizia Zucchi¹⁶⁴, Ferdinando Giannattasio¹⁶⁵, Domenico A. Coviello¹⁶⁶, Cristina Mussini¹⁶⁷, Luisa Tavecchia¹⁶⁸, Lia Crotti^{169,170,171,172}, Marco Rizzi¹⁷³, Maria Teresa La Rovere¹⁷⁴, Simona Sarzi-Braga¹⁷⁵, Maurizio Bussotti¹⁷⁶, Sabrina Ravaglia¹⁷⁷, Rosangela Artuso¹⁷⁸, Antonio Perrella¹⁷⁹, Davide Romani¹⁸⁰, Paola Bergomi¹⁸¹, Emanuele Catena¹⁸¹, Antonella Vincenti¹⁸², Claudio Ferri¹⁸³, Davide Grassi¹⁸³, Gloria Pessina¹⁸⁴, Mario Tumbarello^{123,185}, Massimo Di Pietro¹⁸⁶, Ravaglia Sabrina¹⁸⁷ & Sauro Luchi¹⁸⁸

Admin team lead Simone Furini¹²³ & Simona Dei¹⁸⁹

Analysis team member Elisa Benetti¹²³, Nicola Picchiotti^{119,190}, Maurizio Sanarico¹⁹¹, Stefano Ceri¹⁹², Pietro Pinoli¹⁹², Francesco Raimondi¹⁹³, Filippo Biscarini¹⁹⁴, Alessandra Stella¹⁹⁴, Kristina Zguro¹⁹³, Katia Capitanì^{123,195}, Mattia Cordioli¹⁹⁶, Sara Pigazzini¹², Mattia Cordioli¹⁹⁶, Sara Pigazzini¹⁹², Lindokuhle Nkambule^{176,2} & Marco Tanfoni¹⁹⁹

Data collection member Chiara Fallerini^{121,123}, Sergio Daga^{121,123}, Margherita Baldassarri^{121,123}, Francesca Fava^{121,122,123}, Elisa Frullanti^{121,123}, Floriana Valentino^{121,123}, Gabriella Doddato^{121,123}, Annarita Giliberti^{121,123}, Rossella Tita¹²², Sara Amitrano¹²², Mirella Bruttini^{121,122,123}, Susanna Croci^{121,123}, Ilaria Meloni^{121,123}, Maria Antonietta Mencarelli¹²², Caterina Lo Rizzo¹²², Anna Maria Pinto¹²², Giada Beligni^{121,123}, Andrea Tommasi¹⁴⁷, Laura Di Sarno^{121,123}, Maria Palmieri^{121,123}, Miriam Lucia Carriero^{121,123}, Diana Alaverdian^{121,123}, Stefano Busani¹⁴⁵, Raffaele Bruno^{124,125}, Marco Vecchia¹⁹⁶, Mary Ann Belli¹⁶⁸, Stefania Mantovan¹⁹⁶, Serena Ludovisi¹⁹⁷, Eugenia Quiros-Roldan¹²⁶, Melania Degli Antoni¹²⁶, Isabella Zanella^{198,199}, Matteo Siano¹²⁹, Arianna Emiliozzi¹⁴⁶, Massimiliano Fabbiani¹³⁰, Barbara Rossetti¹³⁰, Laura Bergantini¹³¹, Miriana D'Alessandro¹³¹, Paolo Cameli¹³¹, David Bennett¹³¹, Federico Anedda¹³², Simona Marcantonio¹³², Sabino Scolletta¹³², Susanna Guerrini¹³³, Edoardo Conticini¹³⁴, Bruno Frediani¹³⁴, Chiara Spertilli¹³⁵, Alice Donati¹³⁶, Luca Guidelli¹³⁷, Marta Corridi¹³⁸, Leonardo Croci¹³⁹, Paolo Piacentini¹⁴⁰, Elena Desanctis¹⁴⁰, Silvia Cappelli¹⁴⁰, Agnese Verzuri¹⁴², Valentina Anemoli¹⁴², Alessandro Pancrazzi¹⁴³, Maria Lorubio¹⁴³, Federica Gaia Miraglia¹⁴⁴, Sophie Venturelli¹⁴⁵, Andrea Cossarizza²⁰⁰, Alessandra Vergori¹⁴⁶, Arianna Gabrieli¹²⁹, Agostino Riva^{128,129}, Francesco Paciosi¹⁴⁸, Francesca Andretta¹⁴⁹, Francesca Gatti¹⁵¹, Saverio Giuseppe Parisi²⁰¹, Stefano Baratti²⁰¹, Carmelo Piscopo¹⁵², Roberta Russo^{153,154}, Immacolata Andolfo^{153,154}, Achille Iolascon^{153,154}, Massimo Carella¹⁵⁷, Giuseppe Merla^{153,202}, Gabriella Maria Squeo²⁰², Pamela Raggi²⁰³, Carmen Marciano²⁰³, Rita Perna²⁰³, Matteo Bassetti^{159,204}, Maurizio Sanguinetti^{160,161}, Alessia Giorli¹⁶³, Lorenzo Salerni¹⁶³, Pierpaolo Parravicini¹⁶⁴, Elisabetta Menatti²⁰⁵, Tullio Trotta¹⁶⁵, Gabriella Coiro¹⁶⁵, Fabio Lena²⁰⁶, Enrico Martinelli²⁰⁷, Sandro Mancarella¹⁶⁸, Chiara Gabbi¹⁹¹, Franco Maggiolo¹⁷³, Diego Ripamonti¹⁷³, Tiziana Bachetti²⁰⁸, Claudia Suardi²⁰⁹, Gianfranco Parati^{166,170}, Giordano Bottà²¹⁰, Paolo Di Domenico²¹⁰, Ilaria Rancan¹³⁰, Francesco Bianchi^{23,179}, Riccardo Colombo¹⁸¹, Chiara Barbieri²¹¹, Donatella Acquilini²¹², Elena Andreucci¹⁷⁸, Agostino Riva^{128,129}, Francesco Vladimiro Segala²¹³, Giusy Tiseo²¹¹, Marco Falcone²¹¹, Mirjam Lista^{123,214}, Monica Poscente¹⁸⁴, Oreste De Vivo¹⁶², Paola Petrocelli²¹⁵, Alessandra Guarnaccia¹⁶⁰ & Silvia Baroni²¹⁶

Generation Scotland

Analysis team lead Caroline Hayward²¹⁷

Data collection lead David J. Porteous^{218,219}

Admin team lead Chloe Fawns-Ritchie^{47,218,219}

Analysis team member Anne Richmond²¹⁷

Data collection member Archie Campbell^{218,219}

Genes & Health

Analysis team lead David A. van Heel²²⁰

Data collection lead Karen A. Hunt²²⁰

Admin team lead Richard C. Trembath²²¹

Analysis team member Qin Qin Huang²²² & Hilary C. Martin²²²

Data collection member Dan Mason²²³, Bhavi Trivedi²²⁴ & John Wright²²³

Admin team member Sarah Finer²²⁵

Genes & Health Research Team Shaheen Akhtar²²⁶, Mohammad Anwar²²⁶, Elena Arciero²²⁶, Samina Ashraf²²⁶, Gerome Breen²²⁶, Raymond Chung²²⁶, Charles J. Curtis²²⁶, Maharan Chowdhury²²⁶, Grainne Colligan²²⁶, Panos Deloukas²²⁶, Ceri Durham²²⁶, Sarah Finer²²⁶, Chris Griffiths²²⁶, Qin Qin Huang²²⁶, Matt Hurles²²⁶, Karen A. Hunt²²⁶, Shapna Hussain²²⁶, Kamrul Islam²²⁶, Ahsan Khan²²⁶, Amara Khan²²⁶, Cath Lavery²²⁶, Sang Hyuck Lee²²⁶, Robin Lerner²²⁶, Daniel MacArthur²²⁶, Bev MacLaughlin²²⁶, Hilary Martin²²⁶

Matters arising

Dan Mason²²⁶, Shefa Miah²²⁶, Bill Newman²²⁶, Nishat Safa²²⁶, Farah Tahmasebi²²⁶, Richard C. Trembath²²⁶, Bhavi Trivedi²²⁶, David A. van Heel²²⁶, John Wright²²⁶ & Christopher J. Griffiths²²⁷

Genes for Good

Analysis team lead Albert V. Smith²²⁸

Data collection member Andrew P. Boughton²²⁸, Kevin W. Li²²⁸, Jonathon LeFaive²²⁸ & Aubrey Annis²²⁸

Genome-wide assessment of the gene variants associated with severe COVID-19 phenotype in Iran

Analysis team lead Mari E. K. Niemi¹² & Ahmadreza Niavarani²²⁹

Data collection lead Rasoul Aliannejad²³⁰

Analysis team member Mattia Cordioli⁷, Lindokuhle Nkambul^{17,62} & Bahareh Shariffard²²⁹

Data collection member Ali Amirsavadkouhi²³¹, Zeinab Naderpour²³⁰, Hengameh Ansari Tadi²³², Afshar Etemadi Aleagha²³³, Saeideh Ahmadi²³⁴, Seyed Behrooz Mohseni Moghaddam²³⁵, Alireza Adamsara²³⁶, Morteza Saedi²³⁷, Hamed Abdollahi²³⁸ & Abdolmajid Hosseini²³⁹

Host genetic factors in COVID-19 patients in relation to disease susceptibility, disease severity and pharmacogenomics

Analysis team lead Pajaree Chariyavilaskul^{240,241}

Data collection lead Watsamon Jantarabenjakul^{242,243}

Admin team lead Nattiya Hirankarn^{244,245}

Analysis team member Monpat Chamnanphon^{246,247}, Thitima B. Suttichet²⁴⁶, Vorasuk Shotelersuk^{248,249}, Monnat Pongpanich^{250,251}, Chureerat Phokaew^{249,252,253} & Wanna Chetruengchai^{249,253}

Data collection member Opass Putchareon^{242,254}, Pattama Torvorapanit^{242,254}, Thanyawee Puthanakit^{243,255} & Pintip Suchartlikitwong^{255,256}

Admin team member Voraphoj Nilaratanakul^{257,258} & Pimpayao Sodsa^{244,245}

HUNT

Analysis team lead Ben M. Brumpton^{259,260,261}

Data collection lead Kristian Hveem^{259,260} & Cristen Willer^{262,263,264}

Analysis team member Brooke Wolford^{1262,263,264} & Wei Zhou^{265,266}

Data collection member Tormod Rogne^{267,268,269}, Erik Solligard^{1267,269} & Bjørn Olav Åsvold^{1259,260,261}

Lifelines

Analysis team lead Lude Franke²⁷⁰

Data collection lead Marike Boezen²⁷¹

Analysis team member Patrick Deelen²⁷², Anniqve Claringbould²⁷⁰, Esteban Lopera²⁷⁰, Robert Warmerdam²⁷⁰, Judith. M. Vonk²⁷³ & Irene van Blokland²⁷⁰

Data collection member Pauline Lanting²⁷⁴ & Anil P. S. Ori^{275,276}

Mass General Brigham-Host Vulnerability to COVID-19

Analysis team lead Yen-Chen Anne Feng²⁷⁷ & Josep Mercader^{116,117,278}

Data collection lead Scott T. Weiss²⁷⁹, Elizabeth W. Karlson²⁸⁰, Jordan W. Smoller²⁸¹, Shawn N. Murphy²⁸², James B. Meigs²⁸³ & Ann E. Woolley²⁸⁰

Admin team lead Robert C. Green²⁸⁴

Data collection member Emma F. Perez²⁸⁵

Michigan Genomics Initiative

Analysis team lead Brooke Wolford²⁸⁴

Admin team lead Sebastian Zöllner²²⁸

Analysis team member Jiongming Wang²²⁸ & Andrew Beck²²⁸

Mount Sinai Health System COVID-19 Genomics Initiative

Analysis team lead Laura G. Sloofman^{6,286,287}

Data collection lead Steven Ascolillo²⁸⁸, Robert P. Sebra^{289,290}, Brett L. Collins²⁹¹ & Tess Levy²⁹¹

Admin team lead Joseph D. Buxbaum²⁹¹ & Stuart C. Sealfon⁶

Analysis team member Shea J. Andrews⁶, Daniel M. Jordan^{292,293}, Ryan C. Thompson^{288,294,295}, Kyle Gettler²⁸⁹, Kumardeep Chaudhary^{293,296}, Gillian M. Belbin²⁹⁷, Michael Preuss^{296,298}, Clive Hoggart^{6,299}, Sam Choi³⁰⁰ & Slayton J. Underwood^{6,301}

Data collection member Irene Salib²⁸⁹, Bari Britvan²⁹¹, Katherine Keller²⁹¹, Lara Tang²⁹¹, Michael Peruggia²⁹¹, Liam L. Hiester²⁹¹, Kristi Niblo²⁹¹, Alexandra Aksentjevich²⁹¹, Alexander Labkowsky²⁹¹, Avromie Karp²⁹¹, Menachem Zlatopolsky²⁹¹ & Marissa Zyndorf²⁸⁹

Admin team member Alexander W. Charney³⁰², Noam D. Beckmann²⁸⁸, Eric E. Schadt^{289,290}, Noura S. Abul-Husn²⁹⁷, Judy H. Cho^{293,296}, Yuval Itan^{293,296}, Eimear E. Kenny²⁹⁷, Ruth J. F. Loos^{296,298,303}, Girish N. Nadkarni^{295,296,304,305,306}, Ron Do^{293,296}, Paul O'Reilly³⁰⁰ & Laura M. Huckins³⁰⁷

MyCode Health Initiative

Analysis team lead Manuel A. R. Ferreira³⁰⁸ & Goncalo R. Abecasis³⁰⁸

Data collection lead Joseph B. Leader³⁰⁹ & Michael N. Cantor³⁰⁸

Admin team lead Anne E. Justice³¹⁰ & Dave J. Carey³¹¹

Analysis team member Geetha Chittoor³¹⁰, Navya Shilpa Josyula³¹⁰, Jack A. Kosmicki³⁰⁸, Julie E. Horowitz³⁰⁸ & Aris Baras³⁰⁸

Data collection member Matthew C. Gass³⁰⁹ & Ashish Yadav³⁰⁸

Admin team member Tooraj Mirshahi³¹¹

Netherlands Twin Register

Analysis team lead Jouke Jan Hottenga³¹²

Data collection lead Meike Bartels³¹²

Admin team lead Eco E. J. C. de geus³¹²

Analysis team member Michel M. G. Nivard³¹²

Penn Medicine Biobank

Analysis team lead Anurag Verma³¹³ & Marylyn D. Ritchie³¹³

Admin team lead Daniel Rader³¹³

Analysis team member Binglan Li³¹⁴, Shefali S. Verma³¹³, Anastasia Lucas³¹³ & Yuki Bradford³¹³

Saudi Human Genome Program - COVID19: Host Genomic markers predicting the severity and suitability to COVID-19 in highly consanguineous population

Analysis team lead Malak Abedalthagafi³¹⁵ & Manal Alaamery^{316,317}

Data collection lead Abdurraheem Alshareef³¹⁸ & Mona Sawaji³¹⁹

Admin team lead Salam Massadeh^{316,317} & Abdulaziz AlMalik³²⁰

Analysis team member Saleh Alqahtani^{321,322}, Dona Baraka³²³, Fawz Al Harthi³¹⁵, Ebtahal Alsolm³¹⁵, Leen Abu Safieh³¹⁵, Albandary M. Alowayn³¹⁵, Fatimah Alqubaishi³¹⁵, Amal Al Mutairi³¹⁵ & Serghei Mangul³²⁴

Data collection member Mansour Almutairi^{316,317}, Nora Aljawini³²⁵, Nour Albasher³²⁵, Yaseen M. Arabi³²⁶, Ebrahim S. Mahmoud³²⁶, Amin K. Khattab³²⁷, Roaa T. Halawani³²⁷, Ziab Z. Alahmadey³²⁷, Jehad K. Albakri³²⁷, Walaa A. Felemban³²⁷, Bandar A. Suliman³¹⁸, Rana Hasanato³²³, Laila Al-Awdah³²⁸, Jahad Alghamdi³²⁹, Deema AlZahrani³³⁰, Sameera AlJohani³³¹, Hani Al-Afghani³³², Nouf AlDhawi³³⁰, Hadeel AlBardis³¹⁵, Sarah Alkawai³²⁵, Moneera Alswailm³²⁵, Faisal Almaliki³³⁰, Maha Albeladi³³⁰, Iman Almohammed³²⁵, Eman Barhoush³³³ & Anoud Albader³³⁰

Admin team member Sara Alotaibi³¹⁵, Bader Alghamdi³³⁴, Junghyun Jung³³⁵ & Mohammad S. fawzy³¹⁵

Data collection member May Alrashed³³⁶

The genetic predisposition to severe COVID-19

Analysis team lead Mari E. K. Niemi¹²

Data collection lead Hugo Zeberg^{337,338}

Analysis team member Mattia Cordioli¹⁶, Sara Pigazzini¹² & Lindo Nkambul^{317,339}

Data collection member Robert Frithiof³⁴⁰, Michael Hultström^{340,341}, Miklos Lipcsey^{340,342}, Nicolas Tardif³⁴³, Olav Rooyackers³⁴³, Jonathan Grip³⁴³ & Tomislav Maricic³³⁸

The Norwegian Mother, Father and Child Cohort Study

Analysis team lead Øyvind Helgeland³⁴⁴

Data collection lead Per Magnus³⁴⁵ & Lill-Iren S. Trogstad³⁴⁶

Analysis team member Yunsung Lee³⁴⁵

Admin team member Jennifer R. Harris³⁴⁴

TwinsUK

Analysis team lead Massimo Mangino^{347,348}

Data collection lead Tim D. Spector³⁴⁷

Data collection member Duncan Emma³⁴⁷

UK 100,000 Genomes Project (Genomics England)

Analysis team lead Loukas Moutsianas^{349,350}

Data collection lead Mark J. Caulfield^{349,350,351} & Richard H. Scott^{349,352}

Analysis team member Athanasios Kousathanas³⁵³, Dorota Pasko³⁵³, Susan Walker³⁵³, Alex Stuckey³⁵³, Christopher A. Oshams³⁵³ & Daniel Rhodes³⁵³

Data collection member Tom Fowler³⁵³, Augusto Rendon^{349,354}, Georgia Chan³⁵³ & Prabhu Arumugam³⁵³

UK Biobank

Analysis team lead Tomoko Nakanishi^{22,23,24,25}, Konrad J. Karczewski^{5,19}, Alicia R. Martin^{5,19}, Daniel J. Wilson³⁵⁵ & Chris C. A. Spencer³⁵⁶

Data collection lead Derrick W. Crook³⁵⁷, David H. Wyllie^{357,358} & Anne Marie O'Connell³⁵⁹

Admin team lead J. Brent Richards^{23,27,28}

Analysis team member Guillaume Butler-Laporte^{23,29}, Vincenzo Forgetta²³, Elizabeth G. Atkinson^{5,19}, Masahiro Kana^{5,19,360}, Kristin Tsuo^{5,19,361}, Nikolas Baya^{5,19}, Patrick Turley^{5,19}, Rahul Gupta^{5,19}, Raymond K. Walters^{5,19}, Duncan S. Palmer^{5,19}, Gopal Sarma^{5,19}, Matthew Solomonson^{5,19}, Nathan Cheng^{5,19}, Wenhan Lu^{5,19}, Claire Churchhouse^{5,19}, Jacqueline I. Goldstein^{5,19}, Daniel King^{5,19}, Wei Zhou^{5,19}, Cotton Seed^{5,19}, Mark J. Daly^{2,3,5}, Benjamin M. Neale^{5,19}, Hilary Finucane^{5,19}, Sam Bryant⁵, F. Kyle Satterstrom^{5,19}, Gavin Band³⁶², Sarah G. Earle³⁵⁵, Shang-Kuan Lin³⁵⁵, Nicolas Arning³⁵⁵ & Nils Koelling³⁵⁶

Data collection member Jacob Armstrong³⁵⁵ & Justine K. Rudkin³⁵⁵

Admin team member Shawneeqa Callier³⁶³, Sam Bryant^{5,19} & Caroline Cusick¹⁹

UK Blood Donors Cohort

Analysis team lead Nicole Soranzo^{364,365,366} & Jing Hua Zhao³⁶⁷

Data collection lead John Danesh^{367,368,369,370,371} & Emanuele Di Angelantonio^{367,368,369,370}

Analysis team member Adam S. Butterworth^{367,368,369,370}

Million Veteran Program

Analysis team lead Yan V. Sun^{372,373} & Jennifer E. Huffman³⁷⁴

Data collection lead Kelly Cho³⁷⁵

Admin team lead Christopher J. O'Donnell³⁷⁴, Phil Tsao^{376,377} & J. Michael Gaziano³⁷⁵

Analysis team member Gina Peloso^{374,378}

Data collection member Yuk-Lam Ho³⁷⁵

Vanda COVID

Analysis team lead Sandra P. Smieszek³⁷⁹

Admin team lead Christos Polymeropoulos³⁷⁹, Vasiliios Polymeropoulos³⁷⁹ & Mihael H. Polymeropoulos³⁷⁹

Analysis team member Bartłomiej P. Przychodzen³⁷⁹

Variability in immune response genes and severity of SARS-CoV-2 infection (INMUNGEN-CoV2 study)

Analysis team lead Israel Fernandez-Cadenas³⁸⁰

Data collection lead Anna M. Planas^{381,382}

Analysis team member Jordi Perez-Tur^{383,384,385}, Laia Lluçà-Carol^{380,386}, Natalia Cullèl^{380,387}, Elena Muñío³⁸⁰, Jara Cárcel-Márquez³⁸⁰, Marta L. DeDiego³⁸⁸ & Lara Lloret Iglesias³⁸⁹

Data collection member Alex Soriano³⁹⁰, Veronica Rico³⁹¹, Daiana Agüero³⁹¹, Josep L. Bedini³⁹¹, Francisco Lozano³⁹², Carlos Domingo³⁹¹, Veronica Robles³⁹¹, Francisca Ruiz-Jaén³⁹³, Leonardo Márquez³⁹⁴, Juan Gomez³⁹⁵, Eliecer Coto³⁹⁵, Guillermo M. Albaiceta³⁹⁵, Marta García-Clemente³⁹⁵, David Dalmau³⁹⁶, Maria J. Arranz³⁹⁶, Beatriz Dietl³⁹⁶, Alex Serra-Llovich³⁹⁶, Pere Soler³⁹⁷, Roger Colobrán³⁹⁷, Andrea Martín-Nalda³⁹⁷, Alba Parra Martínez³⁹⁷, David Bernardo³⁹⁸, Silvia Rojo³⁹⁹, Aida Fiz-López³⁹⁸, Elisa Arribas³⁹⁸, Paloma de la Cal-Sabater³⁹⁸, Tomás Segura⁴⁰⁰, Esther González-Villa⁴⁰⁰, Gemma Serrano-Heras⁴⁰¹, Joan Martí-Fàbregas⁴⁰², Elena Jiménez-Xarrié⁴⁰², Alicia de Felipe Mimbres⁴⁰³, Jaime Masjuan⁴⁰³, Sebastian García-Madrona⁴⁰³, Anna Domínguez-Mayoral⁴⁰⁴, Joan Montaner Viallonga⁴⁰⁴ & Paloma Menéndez-Valladares⁴⁰⁴

Women's Genome Health Stud

Analysis team lead Daniel I. Chasman^{405,406}

Data collection lead Howard D. Sesso^{405,406} & JoAnn E. Manson^{405,406}

Admin team lead Julie E. Buring^{405,406} & Paul M. Ridker^{405,406}

Analysis team member Giulianini Franco⁴⁰⁵

Phenotype steering group

Lea Davis⁴³, Andrea Ganna^{2,3,5}, Sulggi Lee⁴⁰⁷, James Priest³⁷⁶, Marco Gori^{119,120}, Vijay G. Sankaran^{3,408}, David van Heel²²⁰, Marika Boezen²⁷¹, J. Brent Richards^{23,27,28}, Tomoko Nakanishi^{22,23,24,25}, Les Biesecker⁴⁰⁹, V. Eric Kerchberger⁴³ & J. Kenneth Baillie^{40,56,410}

COVID-19 HGI corresponding authors

Benjamin M. Neale⁴, Mark Daly^{2,3,5} & Andrea Ganna^{2,3,5}

¹Yale University, New Haven, CT, USA. ²Institute for Molecular Medicine Finland (FIMM), University of Helsinki, Helsinki, Finland. ³Broad Institute of MIT and Harvard, Cambridge, MA, USA. ⁴Massachusetts General Hospital, Broad Institute of MIT and Harvard, Cambridge, MA, USA. ⁵Analytic and Translational Genetics Unit, Massachusetts General Hospital, Boston, MA, USA. ⁶Icahn School of Medicine at Mount Sinai, New York, NY, USA. ⁷Institute for Molecular Medicine Finland (FIMM), University of Helsinki, Helsinki, Finland. ⁸Icahn School of Medicine at Mount Sinai, Genetics and Genomic Sciences, York City, NY, USA. ⁹Centre for Bioinformatics and Data Analysis, Medical University of Białystok, Białystok, Poland. ¹⁰University of Michigan, Ann Arbor, MI, USA. ¹¹Ancestry, Lehi, UT, USA. ¹²Institute for Molecular Medicine Finland (FIMM), Helsinki, Finland. ¹³University of Liege, GIGA-Institute, Liège, Belgium. ¹⁴CHC Mont-Légia, Liège, Belgium. ¹⁵5BHUL (Liège Biobank), CHU of Liège, Liège, Belgium. ¹⁶Institute for Molecular Medicine Finland, University of Helsinki, Helsinki, Finland. ¹⁷Analytic & Translational Genetics Unit, Massachusetts General Hospital, Boston, MA, USA. ¹⁸Stanley Center for Psychiatric Research, Broad Institute of MIT and Harvard, Cambridge, MA, USA. ¹⁹Program in Medical and Population Genetics, Broad Institute of MIT and Harvard, Cambridge, MA, USA. ²⁰CHU of Liege, Liège, Belgium. ²¹University of Liege, Liège, Belgium. ²²Department of Human Genetics, McGill University, Montreal, Quebec, Canada. ²³Lady Davis Institute, Jewish General Hospital, McGill University, Montreal, Quebec, Canada. ²⁴Kyoto-McGill International Collaborative School in Genomic Medicine, Graduate School of Medicine, Kyoto University, Kyoto, Japan. ²⁵Research Fellow, Japan Society for the Promotion of Science, Tokyo, Japan. ²⁶McGill Genome Centre and Department of Human Genetics, McGill University, Montreal, Quebec, Canada. ²⁷Department of Human Genetics, Epidemiology, Biostatistics and Occupational Health, McGill University, Montreal, Quebec, Canada. ²⁸Department of Twin Research, King's College London, London, UK. ²⁹Department of Epidemiology, Biostatistics and Occupational Health, McGill University, Montréal, Québec, Canada. ³⁰Department of Emergency Medicine, McGill University, Montreal, Quebec, Canada. ³¹Emergency Department, Jewish General Hospital, McGill University, Montreal, Quebec, Canada. ³²McGill AIDS Centre, Department of Microbiology and Immunology, Lady Davis Institute for Medical Research, Jewish General Hospital, McGill University, Montreal, Quebec, Canada. ³³McGill Centre for Viral Diseases, Lady Davis Institute, Department of Infectious Disease, Jewish General Hospital, Montreal, Quebec, Canada. ³⁴Research Centre of the Centre Hospitalier de l'Université de Montréal, Montreal, Canada. ³⁵Department of Medicine, Research Centre of the Centre Hospitalier de l'Université de Montréal, Montreal, Canada. ³⁶Department of Medicine, Université de Montréal, Montreal, Canada. ³⁷Department of Medicine and Human Genetics, McGill University, Montreal, Quebec, Canada. ³⁸Department of Intensive Care, Research Centre of the Centre Hospitalier de l'Université de Montréal, Montreal, Quebec, Canada. ³⁹Division of Infectious Diseases, Research Centre of the Centre Hospitalier de l'Université de Montréal, Montreal, Quebec, Canada. ⁴⁰MRC Human Genetics Unit, Institute of Genetics and Cancer, University of Edinburgh, Western General Hospital, Edinburgh, UK. ⁴¹Center for Applied Genomics, Children's Hospital of Philadelphia, Philadelphia, PA, USA. ⁴²Department of Pediatrics, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA. ⁴³Vanderbilt University Medical Center, Nashville, TN, USA. ⁴⁴Centre for Genomic and Experimental Medicine, Institute of Genetics and Cancer,

Matters arising

University of Edinburgh, Western General Hospital, Edinburgh, UK. ⁴⁵Usher Institute, University of Edinburgh, Nine, Edinburgh Bioquarter, Edinburgh, UK. ⁴⁶University of Texas Health, Houston, TX, USA. ⁴⁷Department of Psychology, University of Edinburgh, Edinburgh, UK. ⁴⁸University of North Carolina at Chapel Hill, Chapel Hill, NC, USA. ⁴⁹Center for Applied Genomics, The Children's Hospital of Philadelphia, Philadelphia, PA, USA. ⁵⁰Division of Human Genetics, Department of Pediatrics, The Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA. ⁵¹Divisions of Human Genetics and Pulmonary Medicine, Department of Pediatrics, The Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA. ⁵²Faculty of Medicine, University of Iceland, Reykjavik, Iceland. ⁵³University of Colorado - Anschutz Medical Campus, Aurora, CO, USA. ⁵⁴MRC Human Genetics Unit, Institute of Genetics and Cancer, University of Edinburgh, Western General Hospital, Edinburgh, UK. ⁵⁵Centre for Global Health Research, Usher Institute, University of Edinburgh, Teviot Place, Edinburgh, UK. ⁵⁶The Roslin Institute, The Royal (Dick) School of Veterinary Studies, University of Edinburgh, Edinburgh, UK. ⁵⁷Department of Clinical Pathology, Faculty of Medicine, Mansoura University, Mansoura, Egypt. ⁵⁸Department of Biosciences, School of Science and Technology, Nottingham Trent University, Nottingham, UK. ⁵⁹Genolier Innovation Network and Hub, Swiss Medical Network, Genolier Healthcare Campus, Genolier, Switzerland. ⁶⁰Department of Pediatrics, Faculty of Medicine, Mansoura University, Mansoura, Egypt. ⁶¹Department of Clinical Pathology, Faculty of Medicine, Tanta University, Tanta, Egypt. ⁶²Stanley Center for Psychiatric Research & Program in Medical and Population Genetics, Broad Institute of MIT and Harvard, Cambridge, MA, USA. ⁶³Chest Department, Faculty of Medicine, Mansoura University, Mansoura, Egypt. ⁶⁴Anesthesia, Surgical Intensive Care & Pain Management Department, Faculty of Medicine, Tanta University, Tanta, Egypt. ⁶⁵Department of Medical Biochemistry, Faculty of Medicine, Mansoura University, Mansoura, Egypt. ⁶⁶Department of Surgery, Faculty of Medicine, Mansoura University, Mansoura, Egypt. ⁶⁷Department of Tropical Medicine, Faculty of Medicine, Mansoura University, Mansoura, Egypt. ⁶⁸pediatric and neonatology, Kafr Elzayat General Hospital, Kafr El-Zayat, Egypt. ⁶⁹Chest Department, Faculty of Medicine, Tanta University, Tanta, Egypt. ⁷⁰Pediatrics Department, Faculty of Medicine, Tanta University, Tanta, Egypt. ⁷¹Department of Anaesthesia and Critical Care, Faculty of Medicine, Mansoura University, Mansoura, Egypt. ⁷²Department of Internal Medicine, Faculty of Medicine, Tanta University, Tanta, Egypt. ⁷³Faculty of Science, Tanta University, Tanta, Egypt. ⁷⁴Department of Internal Medicine, Erasmus MC Rotterdam, Rotterdam, The Netherlands. ⁷⁵Department of Epidemiology, Erasmus MC Rotterdam, Rotterdam, The Netherlands. ⁷⁶Estonian Genome Centre, Institute of Genomics, University of Tartu, Tartu, Estonia. ⁷⁷SYNLAB Estonia, University of Tartu, Tartu, Estonia. ⁷⁸Kuressaare Hospital, Kuressaare, Estonia. ⁷⁹University of Tartu, Tartu, Estonia. ⁸⁰Institute of Biomedical and Translational Medicine, University of Tartu, Tartu, Estonia. ⁸¹West Tallinn Central Hospital, Tallinn, Estonia. ⁸²University of Tartu, Tartu University Hospital, Tartu, Estonia. ⁸³Estonian Health Insurance Fund, Tallinn, Estonia. ⁸⁴Tartu University Hospital, Tartu, Estonia. ⁸⁵Department of Health Sciences, University of Leicester, Leicester, UK. ⁸⁶Leicester NIHR Biomedical Research Centre, Leicester, UK. ⁸⁷Department of Respiratory Sciences, University of Leicester, Leicester, UK. ⁸⁸Department of Genetics and Genome Biology, University of Leicester, Leicester, UK. ⁸⁹FinnGen, Helsinki, Finland. ⁹⁰Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland. ⁹¹Public Health, Faculty of Medicine, University of Helsinki, Helsinki, Finland. ⁹²Finnish Institute for Health and Welfare (THL), Helsinki, Finland. ⁹³University of Helsinki, Faculty of Medicine, Clinical and Molecular Metabolism Research Program, Helsinki, Finland. ⁹⁴Institute of Molecular and Clinical Ophthalmology Basel (IOB), Basel, Switzerland. ⁹⁵Department of Ophthalmology, University of Basel, Basel, Switzerland. ⁹⁶Infectious Diseases Service, Department of Medicine, University Hospital and University of Lausanne, Lausanne, Switzerland. ⁹⁷Infectious Diseases Service, Department of Medicine, University Hospital, University of Lausanne, Lausanne, Switzerland. ⁹⁸Centre for Primary Care and Public Health, University of Lausanne, Lausanne, Switzerland. ⁹⁹Division of Infectious Diseases and Hospital Epidemiology, Cantonal Hospital St Gallen, St Gallen, Switzerland. ¹⁰⁰Division of Intensive Care, Geneva University Hospitals and the University of Geneva Faculty of Medicine, Geneva, Switzerland. ¹⁰¹Infectious Disease Service, Department of Internal Medicine, Geneva University Hospital, Geneva, Switzerland. ¹⁰²Clinique de Médecine et spécialités, Infectiologie, HFR-Fribourg, Fribourg, Switzerland. ¹⁰³Infectious Diseases Division, University Hospital Centre of the Canton of Vaud, Hospital of Valais, Sion, Switzerland. ¹⁰⁴Functional Host Genomics of Infectious Diseases, University Hospital and University of Lausanne, Lausanne, Switzerland. ¹⁰⁵Registry COVID, University Hospital and University of Lausanne, Lausanne, Switzerland. ¹⁰⁶Pneumonia prediction using lung ultrasound, University Hospital and University of Lausanne, Lausanne, Switzerland. ¹⁰⁷Center for Primary Care and Public Health (Unisanté), University of Lausanne, Lausanne, Switzerland. ¹⁰⁸Covid-19 Risk Prediction in Swiss ICUs-Trial, Division of Infectious Diseases and Hospital Epidemiology, Cantonal Hospital St Gallen, St Gallen, Switzerland. ¹⁰⁹GCAT-Genomes for Life, Germans Trias i Pujol Health Sciences Research Institute (IGTP), Badalona, Spain. ¹¹⁰Catalan Institute of Oncology, Bellvitge Biomedical Research Institute, Consortium for Biomedical Research in Epidemiology and Public Health and University of Barcelona, Barcelona, Spain. ¹¹¹ISGlobal, Barcelona, Spain. ¹¹²IMIM (Hospital del Mar Medical Research Institute), Barcelona, Spain. ¹¹³Universitat Pompeu Fabra (UPF), Barcelona, Spain. ¹¹⁴CIBER Epidemiologia y Salud Pública (CIBERESP), Madrid, Spain. ¹¹⁵Barcelona Supercomputing Center, Centro Nacional de Supercomputación (BSC-CNS), Life & Medical Sciences, Barcelona, Spain. ¹¹⁶Diabetes Unit and Center for Genomic Medicine, Massachusetts General Hospital, Boston, MA, USA. ¹¹⁷Harvard Medical School, Boston, Massachusetts, USA. ¹¹⁸Barcelona Supercomputing Center, Centro Nacional de Supercomputación (BSC-CNS), Life & Medical Sciences, Barcelona, Spain. ¹¹⁹University of Siena, DIISM-SAILAB, Siena, Italy. ¹²⁰Université Côte d'Azur, Inria, CNRS, I3S, Maasai, Nice, France. ¹²¹Medical Genetics, University of Siena, Siena, Italy. ¹²²Genetica Medica, Azienda Ospedaliero-Universitaria Senese, Siena, Italy. ¹²³Med Biotech Hub and Competence Center, Department of Medical Biotechnologies, University of Siena, Siena, Italy. ¹²⁴Division of Infectious Diseases and Immunology, Department of Medical Sciences and Infectious Diseases, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy. ¹²⁵Department of Internal Medicine and Therapeutics, University of Pavia, Pavia, Italy. ¹²⁶Department of Infectious and Tropical Diseases, University of Brescia and ASST Spedali Civili Hospital, Brescia, Italy. ¹²⁷Chirurgia Vascolare, Ospedale Maggiore di Crema, Crema, Italy. ¹²⁸III Infectious Diseases Unit, ASST-FBF-Sacco, Milan, Italy. ¹²⁹Department of Biomedical and Clinical Sciences Luigi Sacco, University of Milan, Milan, Italy. ¹³⁰Dept of Specialized and Internal Medicine, Tropical and Infectious Diseases Unit, Azienda Ospedaliera Universitaria Senese, Siena, Italy. ¹³¹Unit of Respiratory Diseases and Lung Transplantation, Department of Internal and Specialist Medicine, University of Siena, Siena, Italy. ¹³²Dept of Emergency and Urgency, Medicine, Surgery and Neurosciences, Unit of Intensive Care Medicine, Siena University Hospital, Siena, Italy. ¹³³Department of Medical, Surgical and Neuro Sciences and Radiological Sciences, Unit of Diagnostic Imaging, University of Siena, Siena, Italy. ¹³⁴Rheumatology Unit, Department of Medicine, Surgery and Neurosciences, University of Siena, Policlinico Le Scotte, Siena, Italy. ¹³⁵Department of Specialized and Internal Medicine, Infectious Diseases Unit, San Donato Hospital Arezzo, Arezzo, Italy. ¹³⁶Dept of Emergency, Anesthesia Unit, San Donato Hospital, Arezzo, Italy. ¹³⁷Department of Specialized and Internal Medicine, Pneumology Unit and UTIP, San Donato Hospital, Arezzo, Italy. ¹³⁸Department of Emergency, Anesthesia Unit, Misericordia Hospital, Grosseto, Italy. ¹³⁹Department of Specialized and Internal Medicine, Infectious Diseases Unit, Misericordia Hospital, Grosseto, Italy. ¹⁴⁰Department of Preventive Medicine, Azienda USL Toscana Sud Est, Arezzo, Italy. ¹⁴¹Clinical Chemical Analysis Laboratory, Misericordia Hospital, Grosseto, Italy. ¹⁴²Territorial Scientific Technician Department, Azienda USL Toscana Sud Est, Arezzo, Italy. ¹⁴³Clinical Chemical Analysis Laboratory, San Donato Hospital, Arezzo, Italy. ¹⁴⁴Department of Health Sciences, Clinic of Infectious Diseases, ASST Santi Paolo e Carlo, University of Milan, Milan, Italy. ¹⁴⁵Department of Anesthesia and Intensive Care, University of Modena and Reggio Emilia, Modena, Italy. ¹⁴⁶HIV/AIDS Department, National Institute for Infectious Diseases, IRCCS, Lazzaro Spallanzani, Rome, Italy. ¹⁴⁷Infectious Diseases Clinic, Department of Medicine 2, Azienda Ospedaliera di Perugia and University of Perugia, Santa Maria Hospital, Perugia, Italy. ¹⁴⁸Infectious Diseases Clinic, "Santa Maria" Hospital, University of Perugia, Perugia, Italy. ¹⁴⁹Department of Infectious Diseases, Treviso Hospital, Treviso, Italy. ¹⁵⁰Clinical Infectious Diseases, Mestre Hospital, Venezia, Italy. ¹⁵¹Infectious Diseases Clinic, Belluno Hospital, Viale Europa, Belluno, Italy. ¹⁵²Medical Genetics and Laboratory of Medical Genetics Unit, A.O.R.N. "Antonio Cardarelli", Naples, Italy. ¹⁵³Department of Molecular Medicine and Medical Biotechnology, University of Naples Federico II, Naples, Italy. ¹⁵⁴CEINGE Biotechnologie Avanzate, Naples, Italy. ¹⁵⁵IRCCS SDN, Naples, Italy. ¹⁵⁶Unit of Respiratory Physiopathology, AORN dei Colli, Monaldi Hospital, Naples, Italy. ¹⁵⁷Division of Medical Genetics, Fondazione IRCCS Casa Sollievo della Sofferenza Hospital, San Giovanni Rotondo, Italy. ¹⁵⁸Department of Medical Sciences, Fondazione IRCCS Casa Sollievo della Sofferenza Hospital, San Giovanni Rotondo, Italy. ¹⁵⁹Infectious Diseases Clinic, Policlinico San Martino Hospital, IRCCS for Cancer Research, Genova, Italy. ¹⁶⁰Microbiology, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Catholic University of Medicine, Rome, Italy. ¹⁶¹Department of Laboratory Sciences and Infectious Diseases, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy. ¹⁶²Department of Cardiovascular Diseases, University of Siena, Siena, Italy. ¹⁶³Otolaryngology Unit, University of Siena, Siena, Italy. ¹⁶⁴Department of Internal Medicine, ASST Valtellina e Alto Lario, Sondrio, Italy. ¹⁶⁵First Aid Department, Luigi Curto Hospital, Polla, Salerno, Italy. ¹⁶⁶U.O.C. Laboratorio di Genetica Umana, IRCCS Istituto G. Gaslini, Genova, Italy. ¹⁶⁷Infectious Diseases Clinics, University of Modena and Reggio Emilia, Modena, Italy. ¹⁶⁸U.O.C. Medicina, ASST Nord Milano, Ospedale Bassini, Cinisello Balsamo, Milan, Italy. ¹⁶⁹Department of Cardiovascular, Neural and Metabolic Sciences, Istituto Auxologico Italiano, IRCCS, San Luca Hospital, Milan, Italy. ¹⁷⁰Department of Medicine and Surgery, University of Milano-Bicocca, Milan, Italy. ¹⁷¹Istituto Auxologico Italiano, IRCCS, Center for Cardiac Arrhythmias of Genetic Origin, Milan, Italy. ¹⁷²Istituto Auxologico Italiano, IRCCS, Laboratory of Cardiovascular Genetics, Milan, Italy. ¹⁷³Unit of Infectious Diseases, ASST Papa Giovanni XXIII Hospital, Bergamo, Italy. ¹⁷⁴Department of Cardiology, Istituti Clinici Scientifici Maugeri IRCCS, Institute of Montescano, Pavia, Italy. ¹⁷⁵Istituti Clinici Scientifici Maugeri, IRCCS, Department of Cardiac Rehabilitation, Institute of Tradate (VA), Pavia, Italy. ¹⁷⁶Cardiac Rehabilitation Unit, Fondazione Salvatore Maugeri, IRCCS, Scientific Institute of Milan, Milan, Italy. ¹⁷⁷IRCCS C. Mondino Foundation, Pavia, Italy. ¹⁷⁸Medical Genetics Unit, Meyer Children's University Hospital, Florence, Italy. ¹⁷⁹Department of Medicine, Pneumology Unit, Misericordia Hospital, Grosseto, Italy. ¹⁸⁰Department of Preventive Medicine, Azienda USL Toscana Sud Est, Tuscany, Italy. ¹⁸¹Department of Anesthesia and Intensive Care Unit, ASST Fatebenefratelli Sacco, Luigi Sacco Hospital, Polo Universitario, University of Milan, Milan, Italy. ¹⁸²Infectious Disease Unit, Hospital of Massa, Massa, Italy. ¹⁸³Department of Clinical Medicine, Public Health, Life and Environment Sciences, University of L'Aquila, L'Aquila, Italy. ¹⁸⁴UOSD Laboratorio di Genetica Medica - ASL Viterbo, San Lorenzo, Italy. ¹⁸⁵Department of Medical Sciences, Infectious and Tropical Diseases Unit, Azienda Ospedaliera Universitaria Senese, Siena, Italy. ¹⁸⁶Unit of Infectious Diseases, S.M. Annunziata Hospital, Florence, Italy. ¹⁸⁷IRCCS Mondino Foundation, Pavia, Italy. ¹⁸⁸Infectious Disease Unit, Hospital of Lucca, Lucca, Italy. ¹⁸⁹Health Management, Azienda USL Toscana Sudest, Tuscany, Italy. ¹⁹⁰Department of Mathematics, University of Pavia, Pavia, Italy. ¹⁹¹Independent Researcher, Milan, Italy. ¹⁹²Department of Electronics, Information and Bioengineering (DEIB), Politecnico di Milano, Milano, Italy. ¹⁹³Scuola Normale Superiore, Pisa, Italy. ¹⁹⁴CNR-Consiglio Nazionale delle Ricerche, Istituto di Biologia e Biotecnologia Agraria (IBBA), Milano, Italy. ¹⁹⁵Core Research Laboratory, ISPRO, Florence, Italy. ¹⁹⁶Division of Infectious Diseases and Immunology, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy. ¹⁹⁷Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, Italy. ¹⁹⁸Department of Molecular and Translational Medicine, University of Brescia, Brescia, Italy. ¹⁹⁹Clinical Chemistry Laboratory, Cytogenetics and Molecular Genetics Section, Diagnostic Department, ASST Spedali Civili di Brescia, Brescia, Italy. ²⁰⁰Department of Medical and Surgical Sciences for Children and Adults, University of Modena and Reggio Emilia, Modena, Italy. ²⁰¹Department of Molecular Medicine, University of Padova, Padua, Italy. ²⁰²Laboratory of Regulatory and Functional Genomics, Fondazione IRCCS Casa Sollievo della Sofferenza, San Giovanni Rotondo (Foggia), Foggia, Italy. ²⁰³Clinical Trial Office, Fondazione IRCCS Casa Sollievo della Sofferenza Hospital, San Giovanni Rotondo, Italy. ²⁰⁴Department of Health Sciences, University of Genova, Genova, Italy. ²⁰⁵Oncologia Medica e Ufficio Flussi Sondrio, Sondrio, Italy. ²⁰⁶Local Health Unit-Pharmaceutical Department of Grosseto, Toscana Sud Est Local Health Unit, Grosseto, Italy. ²⁰⁷Department of Respiratory Diseases, Azienda Ospedaliera di Cremona, Cremona, Italy. ²⁰⁸Direzione Scientifica, Istituti Clinici Scientifici Maugeri IRCCS, Pavia, Italy. ²⁰⁹Fondazione per la ricerca Ospedale di Bergamo, Bergamo, Italy. ²¹⁰Allelica Inc, New York, NY, USA. ²¹¹Department of Clinical and Experimental Medicine, Infectious Diseases Unit, University of Pisa, Pisa, Italy. ²¹²Infectious Disease Unit, Santo Stefano Hospital, AUSL Toscana Centro, Prato, Italy. ²¹³Clinic of Infectious Diseases, Catholic University of the Sacred Heart, Rome, Italy. ²¹⁴Medical Genetics, University of Siena, Siena, Italy. ²¹⁵Infectious Disease Unit, Hospital

of Lucca, Lucca, Italy. ²¹⁶Department of Diagnostic and Laboratory Medicine, Institute of Biochemistry and Clinical Biochemistry, Fondazione Policlinico Universitario A. Gemelli IRCCS, Catholic University of the Sacred Heart, Rome, Italy. ²¹⁷MRC Human Genetics Unit, IGC, University of Edinburgh, Edinburgh, UK. ²¹⁸Medical Genetics Section, Centre for Genomic and Experimental Medicine, IGC, University of Edinburgh, Edinburgh, UK. ²¹⁹Generation Scotland, Centre for Genomic and Experimental Medicine, IGC, University of Edinburgh, Edinburgh, UK. ²²⁰Blizard Institute, Queen Mary University of London, London, UK. ²²¹School of Basic and Medical Biosciences, Faculty of Life Sciences and Medicine, King's College London, London, UK. ²²²Medical and Population Genomics, Wellcome Sanger Institute, Hinxton, UK. ²²³Bradford Institute for Health Research, Bradford Teaching Hospitals National Health Service (NHS) Foundation Trust, Bradford, UK. ²²⁴Blizard Institute, Queen Mary University of London, London, UK. ²²⁵Institute of Population Health Sciences, Queen Mary University of London, London, UK. ²²⁶Genes & Health, Blizard Institute, Queen Mary University of London, London, UK. ²²⁷Institute of Population Health Sciences, Queen Mary University of London, London, UK. ²²⁸Department of Biostatistics, University of Michigan, Ann Arbor, MI, USA. ²²⁹Digestive Oncology Research Center, Digestive Disease Research Institute, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran. ²³⁰Department of Pulmonology, School of Medicine, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran. ²³¹Department of Critical Care Medicine, Noorafshar Hospital, Tehran, Iran. ²³²Department of Emergency Intensive Care Unit, School of Medicine, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran. ²³³Department of Anesthesiology, School of Medicine, Amir Alam Hospital, Tehran University of Medical Sciences, Tehran, Iran. ²³⁴Department of Pulmonology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran. ²³⁵Department of Pathology, Parseh Pathology and Genetics Laboratory, Tehran, Iran. ²³⁶Department of Microbiology, Health and Family Research Center, NIOC Hospital, Tehran, Iran. ²³⁷Department of Emergency Medicine, School of Medicine, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran. ²³⁸Department of Anesthesiology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran. ²³⁹Department of Pathology, Faculty of Medicine, Tehran Azad University, Tehran, Iran. ²⁴⁰Clinical Pharmacokinetics and Pharmacogenomics Research Unit, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. ²⁴¹Department of Pharmacology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. ²⁴²Thai Red Cross Emerging Infectious Diseases Clinical Centre, King Chulalongkorn Memorial Hospital, Bangkok, Thailand. ²⁴³Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. ²⁴⁴Immunology Division, Department of Microbiology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. ²⁴⁵Center of Excellence in Immunology and Immune-mediated Diseases, Department of Microbiology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. ²⁴⁶Clinical Pharmacokinetics and Pharmacogenomics Research Unit, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. ²⁴⁷Department of Pathology, Faculty of Medicine, Nakornnayok, Srinakharinwirot University, Bangkok, Thailand. ²⁴⁸Center of Excellence for Medical Genomics, Medical Genomics Cluster, Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. ²⁴⁹Center of Excellence for Genomics and Precision Medicine, King Chulalongkorn Memorial Hospital, The Thai Red Cross Society, Bangkok, Thailand. ²⁵⁰Department of Mathematics and Computer Science, Faculty of Science, Chulalongkorn University, Bangkok, Thailand. ²⁵¹Omic Sciences and Bioinformatics Center, Faculty of Science, Chulalongkorn University, Bangkok, Thailand. ²⁵²Research Affairs, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. ²⁵³Center of Excellence for Medical Genomics, Medical Genomics Cluster, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. ²⁵⁴Division of Infectious Disease, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. ²⁵⁵Center of Excellence in Pediatric Infectious Diseases and Vaccines, Chulalongkorn University, Bangkok, Thailand. ²⁵⁶Department of Microbiology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. ²⁵⁷Division of Infectious Diseases, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. ²⁵⁸Healthcare-associated Infection Research Group STAR (Special Task Force for Activating Research), Chulalongkorn University, Bangkok, Thailand. ²⁵⁹K.G. Jebsen Center for Genetic Epidemiology, Department of Public Health and Nursing, NTNU, Norwegian University of Science and Technology, Trondheim, Norway. ²⁶⁰HUNT Research Center, Department of Public Health and Nursing, NTNU, Norwegian University of Science and Technology, Levanger, Norway. ²⁶¹Clinic of Medicine, St. Olavs Hospital, Trondheim University Hospital, Trondheim, Norway. ²⁶²Division of Cardiovascular Medicine, Department of Internal Medicine, University of Michigan, Ann Arbor, MI, USA. ²⁶³Department of Computational Medicine and Bioinformatics, University of Michigan, Ann Arbor, MI, USA. ²⁶⁴Department of Human Genetics, University of Michigan, Ann Arbor, MI, USA. ²⁶⁵Analytic and Translational Genetics Unit, Massachusetts General Hospital, Boston, Massachusetts, USA. ²⁶⁶Program in Medical and Population Genetics, Broad Institute of Harvard and MIT, Cambridge, Massachusetts, USA. ²⁶⁷Gemini Center for Sepsis Research, Department of Circulation and Medical Imaging, NTNU, Norwegian University of Science and Technology, Trondheim, Norway. ²⁶⁸Department of Chronic Disease Epidemiology and Center for Perinatal, Pediatric and Environmental Epidemiology, Yale School of Public Health, New Haven, CT, USA. ²⁶⁹Clinic of Anaesthesia and Intensive Care, St. Olavs Hospital, Trondheim University Hospital, Trondheim, Norway. ²⁷⁰Department of Genetics, University Medical Center Groningen, University of Groningen, Groningen, Netherlands. ²⁷¹Department of Epidemiology, University Medical Centre Groningen, University of Groningen, Groningen, Netherlands. ²⁷²Department of Genetics, University Medical Centre Groningen, University of Groningen / Department of Genetics, University Medical Centre Utrecht, Utrecht, The Netherlands. ²⁷³Department of Epidemiology, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands. ²⁷⁴University of Groningen, University Medical Center Groningen, Department of Genetics, Groningen, The Netherlands. ²⁷⁵Department of Genetics, University Medical Center Groningen, Groningen, The Netherlands. ²⁷⁶Department of Psychiatry, University Medical Center Groningen, Groningen, The Netherlands. ²⁷⁷Center for Genomic Medicine, Massachusetts General Hospital, Boston, MA, USA. ²⁷⁸Programs in Metabolism and Medical and Population Genetics, Broad Institute of MIT and Harvard, Cambridge, MA, USA. ²⁷⁹Channing Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital, Boston, MA, USA. ²⁸⁰Brigham and Women's Hospital, Boston, MA, USA. ²⁸¹Psychiatric and Neurodevelopmental Genetics Unit, Center for Genomic Medicine, Massachusetts General Hospital, Boston, MA, USA. ²⁸²Department of Neurology, Massachusetts General Hospital, Boston, MA, USA. ²⁸³Division of General Internal Medicine, Massachusetts General Hospital and Department of Medicine, Harvard Medical School and Program in Medical and Population Genetics, Broad Institute, Boston, MA, USA. ²⁸⁴Division of Genetics, Department of Medicine, Brigham and Women's Hospital, Broad Institute of MIT and Harvard, Harvard Medical School, Boston, MA, USA. ²⁸⁵Division of Genetics, Department of Medicine, Brigham and Women's Hospital, Boston, MA, USA. ²⁸⁶Seaver Autism Center for Research and Treatment, York City, NY, USA. ²⁸⁷Department of Psychiatry, Icahn School of Medicine, New York, NY, USA. ²⁸⁸Mount Sinai Clinical Intelligence Center, Department of Genetics and Genomic Sciences, Icahn School of Medicine at Mount Sinai, New York, NY, USA. ²⁸⁹Department of Genetics and Genomic Sciences, Icahn School of Medicine at Mount Sinai, New York, NY, USA. ²⁹⁰Sema4, a Mount Sinai venture, Stamford, CT, USA. ²⁹¹Seaver Autism Center for Research and Treatment, Department of Psychiatry, Icahn School of Medicine at Mount Sinai, New York, NY, USA. ²⁹²Mount Sinai Clinical Intelligence Center, Charles Bronfman Institute for Personalized Medicine, New York, NY, USA. ²⁹³Department of Genetics & Genomic Sciences, Icahn School of Medicine at Mount Sinai, New York, NY, USA. ²⁹⁴Icahn Institute of Data Science and Genomics Technology, New York, NY, USA. ²⁹⁵Mount Sinai Clinical Intelligence Center, New York, NY, USA. ²⁹⁶Charles Bronfman Institute for Personalized Medicine, Icahn School of Medicine at Mount Sinai, New York, NY, USA. ²⁹⁷Institute for Genomic Health, Icahn School of Medicine at Mount Sinai, New York, NY, USA. ²⁹⁸The Mindich Child Health and Development Institute, Icahn School of Medicine at Mount Sinai, New York, NY, USA. ²⁹⁹Pamela Sklar Division of Psychiatric Genomics, Department of Psychiatry, Department of Genetic and Genomic Sciences, New York, NY, USA. ³⁰⁰Pamela Sklar Division of Psychiatric Genomics, Department of Psychiatry, Department of Genetic and Genomic Sciences, Icahn School of Medicine at Mount Sinai, New York, NY, USA. ³⁰¹Seaver Autism Center for Research and Treatment, Department of Psychiatry, New York, NY, USA. ³⁰²Mount Sinai Clinical Intelligence Center, Department of Psychiatry, Department of Genetic and Genomic Sciences, Icahn School of Medicine at Mount Sinai, Mount Sinai, NY, USA. ³⁰³Department of Environmental Medicine and Public Health, Icahn School of Medicine at Mount Sinai, New York, NY, USA. ³⁰⁴The Hasso Plattner Institute of Digital Health at Mount Sinai, New York, NY, USA. ³⁰⁵BioMe Phenomics Center, Icahn School of Medicine at Mount Sinai, New York, NY, USA. ³⁰⁶Department of Medicine, Icahn School of Medicine at Mount Sinai, New York, NY, USA. ³⁰⁷Pamela Sklar Division of Psychiatric Genomics, Seaver Autism Center for Research and Treatment, Department of Psychiatry, Department of Genetic and Genomic Sciences, Icahn School of Medicine at Mount Sinai, New York, NY, USA. ³⁰⁸Regeneron Genetics Center, Tarrytown, NY, USA. ³⁰⁹Phenomic Analytics & Clinical Data Core, Geisinger Health System, Danville, PA, USA. ³¹⁰Department of Population Health Sciences, Geisinger Health System, Danville, PA, USA. ³¹¹Department of Molecular and Functional Genomics, Geisinger Health System, Danville, PA, USA. ³¹²Vrije Universiteit Amsterdam, Amsterdam, UK. ³¹³Department of Genetics, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA, USA. ³¹⁴Department of Biomedical Data Science, Stanford University, Stanford, CA, USA. ³¹⁵Genomics Research Department, Saudi Human Genome Project, King Fahad Medical City and King Abdulaziz City for Science and Technology, Riyadh, Saudi Arabia. ³¹⁶Developmental Medicine Department, King Abdullah International Medical Research Center, King Saud Bin Abdulaziz University for Health Sciences, Ministry of National Guard- Health Affairs, Riyadh, Saudi Arabia. ³¹⁷Saudi Human Genome Project (SHGP), King Abdulaziz City for Science and Technology (KACST), Satellite Lab at King Abdulaziz Medical City (KAMC), Ministry of National Guard Health Affairs (MNG-HA), Riyadh, Saudi Arabia. ³¹⁸College of Applied Medical Sciences, Taibah University, Madina, Saudi Arabia. ³¹⁹Developmental Medicine Department, King Abdullah International Medical Research Center, King Saud Bin Abdulaziz University for Health Sciences, Ministry of National Guard Health Affairs, Riyadh, Saudi Arabia. ³²⁰Life Science and environmental institute, King Abdulaziz City for Science and Technology, Riyadh, Saudi Arabia. ³²¹The Liver Transplant Unit, King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia. ³²²The Division of Gastroenterology and Hepatology, Johns Hopkins University, Baltimore, MD, USA. ³²³Department of Pathology, College of Medicine, King Saud University, Riyadh, Saudi Arabia. ³²⁴Titus Family Department of Clinical Pharmacy, USC School of Pharmacy University of Southern California, Los Angeles, CA, USA. ³²⁵KACST-BWH Centre of Excellence for Biomedicine, Joint Centers of Excellence Program, King Abdulaziz City for Science and Technology (KACST), Riyadh, Saudi Arabia. ³²⁶Ministry of the National Guard Health Affairs, King Abdullah International Medical Research Center and King Saud Bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia. ³²⁷Ohud Hospital, Ministry of Health, Madinah, Saudi Arabia. ³²⁸Pediatric Infectious Diseases, Children's Specialized Hospital, King Fahad Medical City, Riyadh, Saudi Arabia. ³²⁹The Saudi Biobank, King Abdullah International Medical Research Center, King Saud bin Abdulaziz University for Health Sciences, Ministry of National Guard Health Affairs, Riyadh, Saudi Arabia. ³³⁰Developmental Medicine Department, King Abdullah International Medical Research Center, King Saud Bin Abdulaziz University for Health Sciences, King AbdulAziz Medical City, Ministry of National Guard Health Affairs, Riyadh, Saudi Arabia. ³³¹Department of Pathology and Laboratory Medicine, King Abdulaziz Medical City, Ministry of National Guard Health Affairs, King Saud Bin Abdulaziz University for Health Sciences and King Abdullah International Medical Research Center, Riyadh, Saudi Arabia. ³³²Laboratory Department, Security Forces Hospital, General Directorate of Medical Services, Ministry of Interior, Riyadh, Saudi Arabia. ³³³King Abdulaziz City for Science and Technology (KACST), Riyadh, Saudi Arabia. ³³⁴Department of Developmental Medicine, King Abdullah International Medical Research Center, King Saud Bin Abdulaziz University for Health Sciences, King Abdulaziz Medical City, Ministry of National Guard Health Affairs, Riyadh, Saudi Arabia. ³³⁵Titus Family Department of Clinical Pharmacy, USC School of Pharmacy, Los Angeles, CA, USA. ³³⁶Department of Clinical Laboratory Sciences, College of Applied Medical Sciences, King Saud University, Riyadh, Saudi Arabia. ³³⁷Department of Neuroscience, Karolinska Institutet, Stockholm, Sweden. ³³⁸Max Planck Institute for Evolutionary Anthropology, Leipzig, Germany. ³³⁹Stanley Center for Psychiatric Research & Program in Medical and Population Genetics, Cambridge, MA, USA. ³⁴⁰Anesthesiology and Intensive Care Medicine, Department of Surgical Sciences, Uppsala University, Uppsala, Sweden. ³⁴¹Integrative Physiology, Department of Medical Cell Biology, Uppsala University, Uppsala, Sweden. ³⁴²Hedenstierna Laboratory, CIRRUS, Anaesthesiology and Intensive Care Medicine, Department of Surgical Sciences, Uppsala University, Uppsala, Sweden. ³⁴³Division Anaesthesiology and Intensive Care, CLINTEC, Karolinska Institutet, Stockholm, Sweden. ³⁴⁴Department of Genetics and Bioinformatics, Norwegian Institute of Public Health, Oslo, Norway. ³⁴⁵Centre for Fertility and Health, Norwegian Institute of Public Health, Oslo, Norway.

Matters arising

³⁴⁶Department of Method Development and Analytics, Norwegian Institute of Public Health, Oslo, Norway. ³⁴⁷King's College London, Department of Twin Research and Genetic Epidemiology, London, UK. ³⁴⁸NIHR Biomedical Research Centre at Guy's and St Thomas' Foundation Trust, London, UK. ³⁴⁹Genomics England, London, UK. ³⁵⁰Queen Mary University, London, UK. ³⁵¹William Harvey Research Institute, Barts and the London School of Medicine and Dentistry, Queen Mary University of London, London, UK. ³⁵²UCL Great Ormond Street Institute of Child Health, London, UK. ³⁵³Genomics England, London, UK. ³⁵⁴University of Cambridge, London, United Kingdom. ³⁵⁵Big Data Institute, Nuffield Department of Population Health, University of Oxford, Li Ka Shing Centre for Health Information and Discovery, Old Road Campus, Oxford, UK. ³⁵⁶Genomics PLC, King Charles House, Oxford, UK. ³⁵⁷Nuffield Department of Medicine, Experimental Medicine Division, University of Oxford, John Radcliffe Hospital, Oxford, UK. ³⁵⁸Public Health England, Field Service, Addenbrooke's Hospital, Cambridge, UK. ³⁵⁹Public Health England, Data and Analytical Services, National Infection Service, London, UK. ³⁶⁰Program in Bioinformatics and Integrative Genomics, Harvard Medical School, Boston, MA, USA. ³⁶¹Program in Biological and Biomedical Sciences, Harvard Medical School, Boston, MA, USA. ³⁶²Wellcome Centre for Human Genetics, University of Oxford, Roosevelt Drive, Oxford, UK. ³⁶³Department of Clinical Research and Leadership, George Washington University, Washington, DC, USA. ³⁶⁴Department of Human Genetics, The Wellcome Sanger Institute, Wellcome Genome Campus, Hinxton, Cambridge, UK. ³⁶⁵The National Institute for Health Research Blood and Transplant Unit in Donor Health and Genomics, University of Cambridge, Strangeways Research Laboratory, Wort's Causeway, Cambridge, UK. ³⁶⁶Department of Haematology, University of Cambridge, Cambridge Biomedical Campus, Long Road, Cambridge, UK. ³⁶⁷British Heart Foundation Cardiovascular Epidemiology Unit, Department of Public Health and Primary Care, University of Cambridge, Cambridge, UK. ³⁶⁸British Heart Foundation Centre of Research Excellence, University of Cambridge, Cambridge, UK. ³⁶⁹National Institute for Health Research Blood and Transplant Research Unit in Donor Health and Genomics, University of Cambridge, Cambridge, UK. ³⁷⁰Health Data Research UK Cambridge, Wellcome Genome Campus and University of Cambridge, Cambridge, UK. ³⁷¹Department of Human Genetics, Wellcome Sanger Institute, Hinxton, UK. ³⁷²Department of Epidemiology, Emory University Rollins School of Public Health, Atlanta, GA, USA. ³⁷³Atlanta CA Health Care System, North Druid Hills, GA, USA. ³⁷⁴Center for Population Genomics, MAVERIC, VA Boston Healthcare System, Boston, MA, USA. ³⁷⁵MAVERIC, VA Boston Healthcare System,

Boston, MA, USA. ³⁷⁶Stanford University, Stanford, CA, USA. ³⁷⁷Palo Alto VA Healthcare System, Stanford, CA, USA. ³⁷⁸Department of Biostatistics, Boston University School of Public Health, Boston, MA, USA. ³⁷⁹Vanda Pharmaceuticals Inc., Washington, DC, USA. ³⁸⁰Stroke Pharmacogenomics and Genetics, Biomedical Research Institute Sant Pau, Sant Pau Hospital, Barcelona, Spain. ³⁸¹Institute for Biomedical Research of Barcelona (IIBB), National Spanish Research Council (CSIC), Madrid, Spain. ³⁸²Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain. ³⁸³Institute of Biomedicine of Valencia (IBV), CSIC, València, Spain. ³⁸⁴Network Center for Biomedical Research on Neurodegenerative Diseases (CIBERNED), València, Spain. ³⁸⁵Neurology and Genetic Mixed Unit, La Fe Health Research Institute, València, Spain. ³⁸⁶Institute for Biomedical Research of Barcelona (IIBB), National Spanish Research Council (CSIC), Barcelona, Spain. ³⁸⁷Department of Neurology, Hospital Universitari MútuaTerrassa, Fundació Docència i Recerca MútuaTerrassa, Terrassa, Spain. ³⁸⁸Department of Molecular and Cell Biology, Centro Nacional de Biotecnología (CNB-CSIC), Campus Universidad Autónoma de Madrid, Madrid, Spain. ³⁸⁹Instituto de Física de Cantabria (IFCA-CSIC), Santander, Spain. ³⁹⁰Hospital Clínic, IDIBAPS, Barcelona, Spain. ³⁹¹Hospital Clínic, Barcelona, Spain. ³⁹²Hospital Clínic, IDIBAPS, School of Medicine, University of Barcelona, Barcelona, Spain. ³⁹³IDIBAPS, Barcelona, Spain. ³⁹⁴IIBB-CSIC, Barcelona, Spain. ³⁹⁵Servicio de Salud del Principado de Asturias, Oviedo, Spain. ³⁹⁶Hospital Mutua de Terrassa, Terrassa, Spain. ³⁹⁷Hospital Valle Hebrón, Barcelona, Spain. ³⁹⁸Instituto de Biomedicina y Genética Molecular (IBGM), CSIC-Universidad de Valladolid, Valladolid, Spain. ³⁹⁹Hospital Clínico Universitario de Valladolid (SACYL), Valladolid, Spain. ⁴⁰⁰Department of Neurology, University Hospital of Albacete, Albacete, Spain. ⁴⁰¹Research Unit, University Hospital of Albacete, Albacete, Spain. ⁴⁰²Department of Neurology, Biomedical Research Institute Sant Pau (IIB Sant Pau), Hospital de la Santa Creu i Sant Pau, Barcelona, Spain. ⁴⁰³Hospital Universitario Ramón Y Cajal, IRYCIS, Madrid, Spain. ⁴⁰⁴Institute de Biomedicine of Seville, IBIS/Hospital Universitario Virgen del Rocío/CSIC/University of Seville & Department of Neurology, Hospital Universitario Virgen Macarena, Seville, Spain. ⁴⁰⁵Brigham and Women's Hospital, Boston, USA. ⁴⁰⁶Harvard Medical School, Boston, MA, USA. ⁴⁰⁷University of California San Francisco, San Francisco, CA, USA. ⁴⁰⁸Boston Children's Hospital, Boston, MA, USA. ⁴⁰⁹National Institutes of Health, Bethesda, MD, USA. ⁴¹⁰Intensive Care Unit, Royal Infirmary of Edinburgh, Edinburgh, UK. [✉]e-mail: aganna@broadinstitute.org

Reporting Summary

Nature Portfolio 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 Portfolio 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 (n) 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
Only common tests should be described solely by name; describe more complex techniques in the Methods section.
- 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. F , t , r) with confidence intervals, effect sizes, degrees of freedom and P value noted
Give P values as exact values whenever suitable.
- 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 d , Pearson's r), 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

Data analysis https://www.covid19hg.org/). For quality control of genotype data we recommended using the Ripoli pipeline (PMID: 31393554). For genotype phasing and imputation we recommended the TopMed Imputation Server (PMID: 27571263) or Michigan Imputation Server (PMID: 27571263). For genome-wide association study (GWAS), we recommended SAIGE (PMID: 30104761), but some studies used PLINK (PMID: 17701901). Each study then submitted their GWAS summary statistics to the consortium for meta-analysis.
LD score regression v 1.0.1 [PMID: 25642630] was used for heritability and partitioned heritability analyses. Variants for Mendelian randomization instruments were selected using PLINK version 1.90b6.18 (PMID: 17701901). Exposure and outcome datasets were harmonized, and MR statistical analysis conducted using R version 4.0.3. with the R-package TwoSampleMR version 0.5.5 (PMID: 29846171) (which included Fixed-effects IVW analysis (PMID: 24114802), weighted median estimator (WME) (PMID: 27061298), weighted mode based estimator (WMBE) and MR Egger regression (PMID: 26050253)) and additionally MR-PRESSO version 1.0 (PMID: 29686387).
Code availability statement: The code for summary statistics liftover, projection PCA pipeline including precomputed loadings and metaanalysis are available at <https://github.com/covid19-hg/>, the code for Mendelian randomization and genetic correlation pipeline at <https://github.com/marcoralab/MRcovid>, and code for Probabilistic assignment of variants into susceptibility vs. severity effects is at https://github.com/mjpirinen/covid19-hgi_subtypes

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 Portfolio [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 description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our [policy](#)

Summary statistics generated by COVID-19 HGI are available at <https://www.covid19hg.org/results/r6/>. The analyses described here utilize the freeze 6 data. COVID-19 HGI continues to regularly release new data freezes. Summary statistics for non-European ancestry samples are not currently available due to the small individual sample sizes of these groups, but results for 23 loci lead variants are reported in Supplementary Table 4. Individual level data can be requested directly from contributing studies, listed in Supplementary Table 1. We used publicly available data from GTEx (<https://gtexportal.org/home/>), the Neale lab (<http://www.nealelab.is/uk-biobank/>), Finucane lab (<https://www.finucanelab.org>), FinnGen Freeze 4 cohort (https://www.finnngen.fi/en/access_results), and eQTL catalogue release 3 (<http://www.ebi.ac.uk/eql/>).

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	The consortium meta-analysed genome-wide association study (GWAS) summary statistics from any individual study that had included a minimum of 50 cases and 50 controls in their analysis. The cutoff was aimed at reducing noise for the meta-analysis, but also to be inclusive of studies that had not yet accumulated large numbers of COVID-19 patient data. No statistical calculation for adequate sample size was performed, but the results identifying multiple genomic regions at genome-wide significance threshold indicates adequate power for genetic discovery.
Data exclusions	Individual level phenotype and genotype data exclusions were performed by each individual study, following the consortium analysis plan recommendations (www.covid19hg.org). Possible reasons for sample exclusion included removing genetic ancestry outliers within a study (using principal components analysis), poor quality of genetic data or lack of phenotypic data for a sample. The consortium manually examined GWAS summary statistics data submitted by each study (for each submitted analysis separately), including sample size used for analysis, allele frequency check against Gnomad reference panel, and distribution of test statistics. After meta-analysis, the results were checked for heterogeneity variant effects between contributing studies in SupplementaryTable 2
Replication	No replication was performed. The consortium meta-analysed GWAS summary statistics, bringing together as many studies as possible to achieve the largest possible sample size and statistical power for association. this meant that the consortium included most large studies of COVID-19 host genetics that have been performed to date, so it was not possible to perform replication analyses in external cohorts. Therefore we performed manual checks on each study contributing summary statistics before entering them into the meta-analysis. In addition, after meta-analysis, we performed a check for heterogeneity between variant association estimates across studies contributing data. This allowed us to better understand whether the variant effects differed much between individual studies.
Randomization	No randomization was performed because there was no allocation of samples to experimental groups
Blinding	Blinding was not relevant to the study. The case status and severity of symptoms was evaluated for each sample by investigators from each study respectively. The consortium recommended using covariates to control for confounding: age + age ² + sex + age*sex + 20 principal components (obtained using genetic data) + study specific covariates (if any). The consortium meta-analysed summary statistics from these case/control studies, not individual level data. Details of which variables each study used and how the calculated PCs for their analysis are available in Supplementary Table 1.

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

Methods

n/a	Included in the study
<input checked="" type="checkbox"/>	<input type="checkbox"/> Antibodies
<input checked="" type="checkbox"/>	<input type="checkbox"/> Eukaryotic cell lines
<input checked="" type="checkbox"/>	<input type="checkbox"/> Palaeontology and archaeology
<input checked="" type="checkbox"/>	<input type="checkbox"/> Animals and other organisms
<input type="checkbox"/>	<input checked="" type="checkbox"/> Human research participants
<input checked="" type="checkbox"/>	<input type="checkbox"/> Clinical data
<input checked="" type="checkbox"/>	<input type="checkbox"/> Dual use research of concern

n/a	Included in the study
<input checked="" type="checkbox"/>	<input type="checkbox"/> ChIP-seq
<input checked="" type="checkbox"/>	<input type="checkbox"/> Flow cytometry
<input checked="" type="checkbox"/>	<input type="checkbox"/> MRI-based neuroimaging

Human research participants

Policy information about [studies involving human research participants](#)

Population characteristics

Summary statistics from 60 independent studies were included in consortium meta-analyses. Mean age of cases across studies was 53.36 years. The effective sample size for genetic ancestry populations for Sars-CoV2 reported infection was: n=6147 Middle Eastern; n=23391 South Asian; 13152 East Asian; 39571 African; 39817 Ad-mixed American; 440696 European. Population characteristics regarding age, sex and exact case and control sample numbers for each contributing study are given in Supplementary Table 1.

Recruitment

The consortium pre-defined phenotype criteria for cases and controls, but the specific recruitment was carried out independently by each contributing study. COVID-19 disease status (critical illness, hospitalization status) was assessed following the Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (PMID: 32358325). The critically ill COVID-19 group included patients who were hospitalized due to symptoms associated with laboratory-confirmed SARSCoV-2 infection and who required respiratory support or whose cause of death was associated with COVID-19. The hospitalized COVID-19 group included patients who were hospitalized due to symptoms associated with laboratory-confirmed SARS-CoV-2 infection. The reported infection cases group included individuals with laboratory-confirmed SARSCoV-2 infection or electronic health record, ICD coding or clinically confirmed COVID-19, or self-reported COVID-19 (e.g. by questionnaire), with or without symptoms of any severity. Genetic ancestry-matched controls for the three case definitions were sourced from population-based cohorts, including individuals whose exposure status to SARS-CoV-2 was either unknown or infection-negative for questionnaire/electronic health record based cohorts.

Ethics oversight

Ethical statements for each contributing study are given in Supplementary Table 1.

Note that full information on the approval of the study protocol must also be provided in the manuscript.