Sleep apnoea is a risk factor for severe COVID-19

Satu Strausz,1,2,3 Tuomo Kiiskinen,1,4 Martin Broberg,1 Sanni Ruotsalainen,1 Jukka Koskela,1,5 Adel Bachour,6 FinnGen, Aarno Palotie,1,5,7 Tuula Palotie,2,3 Samuli Ripatti,1,5,8 Hanna M. Ollila1,5,9

ABSTRACT

Background Obstructive sleep apnoea (OSA) is associated with higher body mass index (BMI), diabetes, older age and male gender, which are all risk factors for severe COVID-19. We aimed to study if OSA is an independent risk factor for COVID-19 infection or for severe COVID-19.

Methods OSA diagnosis and COVID-19 infection were extracted from the hospital discharge, causes of death and infectious diseases registries in individuals who participated in the FinnGen study (n=260 405). Severe COVID-19 was defined as COVID-19 requiring hospitalisation. Multivariate logistic regression model was used to examine association. Comorbidities for either COVID-19 or OSA were selected as covariates. We performed a meta-analysis with previous studies.

Results We identified 445 individuals with COVID-19, and 38 (8.5%) of them with OSA of whom 19 out of 91 (20.9%) were hospitalised. OSA associated with COVID-19 hospitalisation independent from age, sex, BMI and comorbidities (p-unadjusted=5.13x10^{-5}, OR-adjusted=2.93 (95% CI 1.02 to 8.39), p-adjusted=0.045). OSA was not associated with the risk of contracting COVID-19 (p=0.25). A meta-analysis of OSA and severe COVID-19 showed association across 15 835 COVID-19 positive controls, and n=1294 patients with OSA with severe COVID-19 (OR=2.37 (95% 1.14 to 4.95), p=0.021).

Conclusion Risk for contracting COVID-19 was the same for patients with OSA and those without OSA. In contrast, among COVID-19 positive patients, OSA was associated with higher risk for hospitalisation. Our findings are in line with earlier works and suggest OSA as an independent risk factor for severe COVID-19.

INTRODUCTION

COVID-19 is a severe respiratory disease caused by SARS-CoV-2 virus infection. A subset of patients face hospitalisation, respiratory failure or even death. The severity of COVID-19 is highly age dependent but also evidenced by the number of individuals that receive hospital and intensive care treatment.1,2 Finland has had a relatively small number of COVID-19 cases in the spring of 2020. However, approximately 1%–6% of those tested positive for the virus in Finland received hospital or intensive care treatment.3 These percentages are similar to those reported globally.1,2 Severe COVID-19 outcome is mediated primarily through respiratory distress.1,5 Risk factors for severe COVID-19 have been identified as older age, male sex, obesity, diabetes, cardiovascular disease and poor lung function.6 In addition, other respiratory diseases have been listed as potential contributors for COVID-19 severity. Indeed, there are studies suggesting that obstructive sleep apnoea (OSA) may be a risk factor for severe COVID-19.7-12 Such risk would have substantial effect as OSA is a common disease affecting at least 8% of the population with higher prevalence in older age groups reaching to over 20% in individuals over 60 years of age.13 The disease aetiology of OSA is characterised by repetitive apnoea-hypopnea cycles during sleep causing shortness of breath which can be associated with sometimes severe oxygen desaturation, sleep disruption and increase in systolic and diastolic blood pressure.14 The known risk factors for OSA include obesity, high age, male sex and craniofacial and upper airway structure variations and anomalies.15 Similarly, OSA is associated with increased risk for cardiovascular mortality, especially if not treated. Finally, it is essential to note that treatment exists for the majority of patients with OSA so that night-time breathing can be...
supported by continuous positive airway pressure (CPAP) or mandibular advancement device (MAD). This treatment substantially decreases the risk for cardiovascular events and death.\(^{16,17}\) Recently, questions have been raised about whether OSA constitutes a high risk for COVID-19 infection or COVID-19 hospitalisation.

We specifically aimed at evaluating if OSA associates with the risk for severe COVID-19 infection independently of other potential risk factors including age, sex, body mass index (BMI), hypertension, diabetes (including type 1 and type 2 diabetes), coronary heart disease (CHD) asthma and chronic obstructive pulmonary disease (COPD), and also whether the risk for contracting COVID-19 is elevated among patients with OSA.

**METHODS**

**Study sample set**

FinnGen (https://www.finngen.fi/en) is a large biobank study that aims to genotype 500 000 Finns including two types of biobank collections: (1) population-based epidemiological cohorts and (2) mostly disease-based collections in all University Hospitals in Finland (online supplemental table 1). FinnGen combines these data with longitudinal registry data that record healthcare events over the entire lifespan including the National Hospital Discharge Registry (available from 1968), the Causes of Death Registry (available from 1969), the National Infectious Diseases Registry (available from 1995) and the Medication Reimbursement Registry (available from 1995), all these using unique national personal identification codes, for the whole population of Finland for lifetime information since the start of each registry. FinnGen has harmonised data from these registries of 260 405 Finnish individuals. Registry data were available from the beginning of the registry until 31 December 2018 and Infectious Registry data until 30 October 2020. In addition, demographic and anthropometric data of BMI and smoking status are included.

The information of COVID-19 positive individuals was collected from The National Infectious Diseases Registry and the infection was verified by laboratory test using PCR testing. Data for risk factors, comorbidities and OSA diagnosis were obtained from the National Hospital Discharge Registry, the Causes of Death Registry and the Medication Reimbursement Registry, where the clinical endpoints had been generated using International Classification of Diseases codes for OSA, hypertension, diabetes (including type 1 and type 2 diabetes), CHD, asthma and COPD (online supplemental table 2).

Treatment information concerning OSA was collected from the patient records of Heart and Lung Center or Department of Oral and Maxillofacial Diseases, Helsinki University Hospital (HUH), Finland.

The diagnosis in this special healthcare derived data for OSA is typically based on the following criteria: subjective symptoms, clinical examination and sleep registration applying Apnoea-Hypopnea Index (AHI) $>5$ per hour for polysomnography or respiratory event index $>5$ per hour for out-of-centre sleep study.

For the meta-analysis, estimates were collected from the previous studies\(^ {2-9}\) concerning the role of OSA on COVID-19 hospitalisation.

**Statistical methods**

Differences in baseline demographics and clinical characteristics were tested using on $\chi^2$ tests. Fisher’s exact test was used if the expected cell size was $\leq 5$. For continuous variables, Student’s t-test was used. We considered $p<0.05$ as statistically significant, and all tests were two sided (tables 1 and 2). All $p$ values based on forementioned tests are Bonferroni corrected. Logistic regression was used to calculate OR between hospitalised and non-hospitalised groups. Model 1 was adjusted for age and

| Table 1 Comparison of the baseline characteristics among COVID-19 positive individuals |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|
|                                | All n=445       | Non-hospitalised n=354 | Hospitalised n=91 | $P_{\text{unadjusted}}$ |
| Age (mean in years, SD)        | 52.7 (17.4)     | 49.3 (16.3)       | 65.9 (14.8)      | 1.06×10$^{-15}$* |
| Sex (male) (N, %)              | 166 (37.3)      | 133 (37.6)        | 33 (36.3)        | 1               |
| OSA (N, %)                     | 38 (8.5)        | 19 (5.4)          | 19 (20.9)        | 5.13×10$^{-5}$*  |
| BMI (mean kg/m$^2$, SD)        | 27.13 (5.44)    | 26.54 (5.20)      | 29.25 (5.78)     | 0.014*          |
| Hypertension (N, %)            | 79 (17.8)       | 40 (11.3)         | 39 (42.9)        | 5.03×10$^{-11}$* |
| Diabetes (N, %)                | 46 (10.3)       | 23 (6.5)          | 23 (25.3)        | 3.45×10$^{-6}$*  |
| CHD (N, %)                     | 21 (4.7)        | 9 (2.5)           | 12 (13.2)        | 5.20×10$^{-4}$*  |
| Asthma/COPD                    | 54 (12.1)       | 40 (11.3)         | 14 (15.4)        | 1               |

Differences and associations between non-hospitalised and hospitalised COVID-19 positive individuals. Baseline demographics and clinical characteristics $P_{\text{unadjusted}}$ values were based on $\chi^2$ test. For continuous variables, we used Student’s t-test. BMI was measured of 264 participants including 206 non-hospitalised and 58 hospitalised individuals.

*Statistically significant.

BMI, body mass index; CHD, coronary heart disease; COPD, chronic obstructive pulmonary disease; OSA, obstructive sleep apnoea.
sex. Model 2 was adjusted for BMI in addition to covariates of Model 1. Model 3 was adjusted for BMI, hypertension, diabetes, CHD, asthma and COPD in addition to covariates of Model 1. Similarly between COVID-19-positive and non-COVID-19 groups.

Our results and previous findings from the corresponding studies were pooled together forming a meta-analysis using restricted maximum likelihood estimation of the random effect model in the Metagen R.

The merged data consisted of 15,835 COVID-19-positive individuals including 1294 patients with OSA.

The R statistical package (V 4.0.2) was used for all analyses (www.r-project.org).

### Patient and public involvement

Patients and public were not involved in the designing process of this study. The patients will not be informed individually of the study results otherwise than through possible media coverage.

### RESULTS

The data included 260,405 Finnish individuals from FinnGen Data Freeze 6 with 445 patients with COVID-19. Of them, 38 (8.5%) had OSA. Severe COVID-19 cases (n=91) included 19 (20.9%) patients with OSA. Severe COVID-19 was defined as an infection requiring hospitalisation.

Of all patients with COVID-19 diagnosis (n=445, 37.3% male, mean age 52.7 years) 38 patients also had OSA diagnosis (8.5%, 50.0% male, mean age 61.3 years). (Tables 1 and 2). This reflects a similar prevalence of OSA diagnoses in COVID-19 infected as in the normal population in FinnGen, where prevalence is 8%. Ninety-one (20.4%) patients required hospitalisation (36.3% male, mean age 65.9 years) including 19 patients with OSA.

Prevalence of OSA (p=5.13×10⁻⁵), hypertension (p=5.03×10⁻¹), diabetes (p=3.45×10⁻⁶) and CHD (p=5.20×10⁻⁴) were statistically significantly higher in the hospitalised group. Similarly, age and BMI were higher among hospitalised individuals (p=1.06×10⁻⁵, p=0.014, respectively; Table 1).

To evaluate the performance of the diagnostic events, we compared the main risk factors among patients with COVID-19 between individuals with OSA (n=38) and those who did not have OSA diagnosis (n=407). Patients with OSA were statistically significantly older and their BMI was higher (mean age 61.3 years, BMI 31.15 kg/m², p=5.60×10⁻⁴, p=3.38×10⁻³, respectively) than non-OSA individuals (mean age 51.9 years, BMI 26.71 kg/m²). Also, comorbidities were more prevalent among OSA individuals (p=1.74×10⁻⁴) and they faced hospitalisation more often (p=3.21×10⁻⁵). We did not observe differences in risk factors when comparing non-hospitalised (n=19, male 63.2%, mean age 56.3 years) and hospitalised patients with OSA (n=19, male 36.8%, mean age 66.3 years; Table 2). Furthermore, 7/19 patients with OSA were hospitalised due to COVID-19 did not have any other disease comorbidities. We did not observe significant differences concerning age or BMI between individuals who had only OSA as a comorbidity or also

### Table 2 Description of patients with COVID-19 with or without obstructive sleep apnoea (OSA) and a comparison between non-hospitalised and hospitalised patients with OSA

<table>
<thead>
<tr>
<th></th>
<th>Non-OSA n=407</th>
<th>OSA n=38</th>
<th>P value</th>
<th>OSA Non-hospitalised n=19</th>
<th>OSA hospitalised n=19</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (mean in years, SD)</strong></td>
<td>51.9 (17.5)</td>
<td>61.3 (12.9)</td>
<td>5.60×10⁻⁴</td>
<td>56.3 (11.0)</td>
<td>66.3 (12.9)</td>
<td>0.057</td>
</tr>
<tr>
<td><strong>Sex (male) (N, %)</strong></td>
<td>147 (36.1)</td>
<td>19 (50.0)</td>
<td>0.645</td>
<td>12 (63.2)</td>
<td>7 (36.8)</td>
<td>0.776</td>
</tr>
<tr>
<td><strong>BMI (mean kg/m², SD)</strong></td>
<td>26.71 (5.27)</td>
<td>31.15 (5.56)</td>
<td>3.38×10⁻³</td>
<td>30.91 (5.58)</td>
<td>31.37 (5.77)</td>
<td>1</td>
</tr>
<tr>
<td><strong>Comorbidities or outcomes (N, %)</strong></td>
<td>118 (29.0)</td>
<td>24 (46.3)</td>
<td>1.74×10⁻⁴</td>
<td>12 (63.2)</td>
<td>12 (63.2)</td>
<td>1</td>
</tr>
<tr>
<td><strong>Hospitalised (N, %)</strong></td>
<td>72 (17.7)</td>
<td>19 (50.0)</td>
<td>3.21×10⁻⁵</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Differences between non-OSA versus OSA individuals and non-hospitalised patients with OSA versus hospitalised patients with OSA among COVID-19-positive individuals. 7/19 patients with hospitalisation had OSA diagnosis but did not have any other disease comorbidities. P values were based on χ² test. Fisher’s exact test was used if the sample size was ≤5. For continuous variables, we used Student’s t-test. BMI was measured of 264 participants including 239 non-OSA and 25 OSA individuals. Comorbidities and outcomes=hypertension, diabetes, coronary heart disease, asthma, chronic obstructive pulmonary disease.

*Statistically significant.

BMI, body mass index.

### Table 3 ORs associating obstructive sleep apnoea with severe COVID-19

<table>
<thead>
<tr>
<th>OR</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1</td>
<td>3.85</td>
<td>1.82 to 8.13</td>
</tr>
<tr>
<td>Model 2</td>
<td>3.45</td>
<td>1.27 to 9.35</td>
</tr>
<tr>
<td>Model 3</td>
<td>2.93</td>
<td>1.02 to 8.39</td>
</tr>
</tbody>
</table>

Model 1 is adjusted for age and sex. Model 2 is adjusted for body mass index (BMI) in addition to covariates of Model 1. Model 3 is adjusted for BMI, hypertension, diabetes, coronary heart disease, asthma and chronic obstructive pulmonary disease in addition to covariates of model 1.

*Statistically significant.
patients with OSA treated in Heart and Lung Center or Department of Oral and Maxillofacial Diseases, HUH, Finland by the end of October 2020. The mean age of the COVID-19 positive patients with OSA was 55.1 years, mean BMI was 35.08 kg/m² and 9 (81.8%) patients were male. Mean AHI was 43.3 events per hour (table 4) and all 11 patients had either moderate (AHI≥15 but<30 events per hour) or severe (AHI≥30 events per hour) OSA; 9 out of 11 had severe OSA and 2 out of 11 had moderate OSA. 8/11 had treated OSA; 7 patients had CPAP therapy and 1 patient had MAD. CPAP-treated patients used their appliances 98% of the nights with 6.3 hours mean time used. Mean AHI during treatment was 1.86 events/hour prior to the COVID-19 infection. Despite of the OSA treatment, all 11 patients required hospital treatment caused by pneumonia or other COVID-19 caused symptoms, such as high fever. All patients needed non-invasive ventilation and two required intubation. Treatment time in hospital was 15 days (mean, table 4).

**DISCUSSION**

Here, we examined the role of OSA as a risk factor for COVID-19 leading to hospitalisation. Our analyses revealed 2.93-times higher risk for COVID-19 hospitalisation in patients with OSA, independently of BMI and other known risk factors for OSA, or those for severe

---

**Table 4 Healthcare data characteristics of individuals with obstructive sleep apnoea contracted with COVID-19**

<table>
<thead>
<tr>
<th>n=11</th>
<th>Age (mean in years)</th>
<th>55.1 (8.0)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male, N, %)</td>
<td>9 (81.8)</td>
<td></td>
</tr>
<tr>
<td>BMI (mean kg/m², SD)</td>
<td>35.08 (5.96)</td>
<td></td>
</tr>
<tr>
<td>Diabetes (N, %)</td>
<td>3 (27.3)</td>
<td></td>
</tr>
<tr>
<td>Hypertension (N, %)</td>
<td>7 (63.6)</td>
<td></td>
</tr>
<tr>
<td>CHD (N, %)</td>
<td>3 (27.3)</td>
<td></td>
</tr>
<tr>
<td>CPAP (N, %)</td>
<td>7 (63.6)</td>
<td></td>
</tr>
<tr>
<td>MAD (N, %)</td>
<td>1 (9.1)</td>
<td></td>
</tr>
<tr>
<td>AHI (mean, events per hour)</td>
<td>43.3 (20.6)</td>
<td></td>
</tr>
<tr>
<td>ODI (mean, events per hour)</td>
<td>39.6 (15.7)</td>
<td></td>
</tr>
<tr>
<td>SpO₂ mean (mean%, SD)</td>
<td>91.0 (3.3)</td>
<td></td>
</tr>
<tr>
<td>SpO₂ min (mean%, SD)</td>
<td>79.4 (8.3)</td>
<td></td>
</tr>
<tr>
<td>AHI with CPAP (mean, events per hour)</td>
<td>1.86 (2.07)</td>
<td></td>
</tr>
<tr>
<td>ICU (N, %)</td>
<td>3 (27.3)</td>
<td></td>
</tr>
<tr>
<td>NIV (N, %)</td>
<td>11 (100)</td>
<td></td>
</tr>
<tr>
<td>Intubation (N, %)</td>
<td>2 (18.2)</td>
<td></td>
</tr>
<tr>
<td>Treatment time in hospital (mean in days, SD)</td>
<td>15 (8.6)</td>
<td></td>
</tr>
</tbody>
</table>

AHI, Apnoea-Hypopnea Index; BMI, body mass index; CHD, coronary heart disease; CPAP, continuous positive airway pressure; ICU, intensive care unit; MAD, mandibular advancement devise; NIV, non-invasive ventilation; ODI, oxygen desaturation index; SpO₂, oxygen saturation.

**Figure 1** Forest plots of obstructive sleep apnoea (OSA) and the risk of hospitalisation due to COVID-19. The evidence is combined using random-effect meta-analysis. The data consisted of 15 835 COVID-19 positive individuals including 1294 patients with OSA. (A) The model is adjusted for age and sex, and ethnic background if available. *Cariou et al* study’s primary outcome was defined as tracheal intubation and/or death within 7 days of admission. (B) The model is adjusted for age, sex and BMI. **Maas et al** study is adjusted for diabetes and hypertension in addition to forementioned covariates.
COVID-19 suggesting that OSA is an independent risk factor for COVID-19.

Indeed, our findings are well in line with earlier works on COVID-19 comorbidities and OSA. Three studies have examined the association between COVID-19 and OSA before. Despite different endpoint definitions (contracting COVID-19, severity of the disease, mechanical ventilation, and death), these studies share similar findings with ours. All studies showed a significant association with COVID-19 severity and OSA.7–9 However, only one study showed a statistically significant association between OSA and severe COVID-19 after adjusting for BMI.9 These findings suggest that while OSA is likely a risk factor for COVID-19, evaluating the magnitude of this association would benefit from harmonised analyses across different cohorts where comorbidities are similarly assessed.

Building on these studies, we set to test the role of OSA on COVID-19 hospitalisation. In our study, patients with OSA had 2.93 times higher risk of being hospitalised and the estimate was comparable and independent of the risk in diabetes patients, where elevated risk has been reported earlier for severe COVID-19.19 There are at least two potential pathological mechanisms how OSA may relate to severe COVID-19. First, individuals with OSA often have one or more comorbidities that are known risk factors for severe COVID-19. For example, high BMI increases the risk for severe COVID-19. Furthermore, OSA exacerbates the effects of many underlying risk factors increasing blood pressure. Second, OSA may worsen the core symptoms of severe COVID-19, especially during the night, when decreased oxygen saturation levels occur in OSA.14 Our findings together with earlier reports suggest that OSA should be taken into account when assessing who will develop life-threatening complications of COVID-19 infection.

In addition, we collected treatment information concerning OSA of 11 patients who had contracted COVID-19. Despite of the OSA treatment, patients developed a severe form of COVID-19 and all patients required hospital care suggesting OSA as a risk factor even if treated.

Finally, based on our results and previous studies,7–9 we set a meta-analysis to strengthen the role of OSA on COVID-19 hospitalisation. We were able to establish OSA as a risk factor and show that the effect is related to COVID-19 severity indicating over 2-fold risk.

Our findings should be interpreted in the context that registry-based ascertainment through hospitalisation may miss non-hospitalised OSA cases (false negatives). In addition, the population prevalence of OSA is larger than the observed prevalence as OSA is still underdiagnosed in Finland. This may affect to our findings. The high percentage of individuals in hospitals likely reflect the age distribution of the first wave patients in Finland, where infections took place in individuals approximately 50 years of age, and selective testing in those that had clear or severe symptoms. Similarly, early on the testing was targeted towards older individuals and to those with comorbidities, as not enough testing capacity was available early in the spring 2020. Although sufficient capacity and different strategies are in place now, the number of patients with mild COVID-19 infection may have not been recorded in the registries from the early spring 2020. Finally, compared with other countries there have been relatively small numbers of COVID-19 infections in Finland till the end of October 2020 when these data were curated. Therefore, while the effect estimates are comparable to other studies on OSA and COVID-19, the confidence intervals are relatively large due to the smaller total number of COVID-19 positive individuals in Finland and in the study sample: less than 500 patients compared with several hundred in other studies. Also, FinnGen represents older population (mean 58.6 years) than the average age (mean 42.9 years) in Finland.20

In conclusion, patients with OSA have the same risk of contracting COVID-19 than non-OSA individuals. Meanwhile, in this study, patients with OSA had 2.93 times higher risk to be hospitalised when affected by COVID-19 than non-OSA individuals. Our findings may suggest that, in assessment of patients with suspected or confirmed COVID-19 infection, OSA should be recognised as one of the comorbidity risk factors for developing a severe form of the disease. We believe that our finding may help in identifying high-risk individuals for severe forms of COVID-19 infection and therefore screening for previous indications of OSA could be beneficial among individuals testing positive for the virus.

Author affiliations
1 Institute for Molecular Medicine Finland (FIMM), University of Helsinki, Helsinki, Finland
2 Orthodontics, Department of Oral and Maxillofacial Diseases, Clinicum, Faculty of Medicine, University of Helsinki, Helsinki, Finland
3 Department of Oral and Maxillofacial Diseases, Helsinki University Hospital (HUH), Helsinki, Finland
4 Finnish Institute for Health and Welfare, Helsinki, Finland
5 Broad Institute of MIT and Harvard, Cambridge, MA, USA
6 Sleep Unit, Heart and Lung Center, Helsinki University Hospital (HUH), Helsinki, Finland
7 Analytic and Translational Genetics Unit (ATGU), Department of Medicine, Department of Neurology and Department of Psychiatry, Massachusetts General Hospital, Boston, Massachusetts, USA
8 Department of Public Health, University of Helsinki, Helsinki, Finland
9 Stanford University School of Medicine, Palo Alto, CA, USA

Correction notice This article has been corrected since it first published. The provenance and peer review statement has been included.

Acknowledgements The authors would like to thank all participants of the FinnGen study for their generous participation. Patients and control subjects in FinnGen provided informed consent for biobank research, based on the Finnish Biobank Act. Alternatively, older research cohorts, collected prior the start of FinnGen (in August 2017), were collected based on study-specific consents and later transferred to the Finnish biobanks after approval by Fimea, the National Supervisory Authority for Welfare and Health. Recruitment protocols followed the biobank protocols approved by Fimea. The Coordinating Ethics Committee of the Hospital District of Helsinki and Uusimaa (HUS) approved the FinnGen study protocol Nr HUS/990/2017.

Contributors HO is the guarantor of the manuscript, TK, HO, SR and SS conceived the study and designed the study protocol. TK, HO and SS conducted the literature review, statistical analysis and drafted the manuscript. MB and SHu contributed statistical analysis and TK phenotyped study samples. AB, MB, JK, SR, SRu, AP, TP
and SR reviewed the manuscript for intellectual content, made revisions as needed and approved the final version for publication. HQ, TP and SR supervised the study.

Funding  SR was supported by the Academy of Finland Center of Excellence in Complex Disease Genetics (Grant No 312062), the Finnish Foundation for Cardiovascular Research, the Sigrid Juselius Foundation and University of Helsinki HLIFE Fellow and Grand Challenge grants and Juho Vainio Foundation & Academy of Finland Covid-19 research funding. AP was supported by the Academy of Finland Center of Excellence in Complex Disease Genetics (Grant No 312074), and the Sigrid Juselius Foundation. HMO was supported by the Academy of Finland (Grant No 309643, 340539), Oskar Öfflund foundation, Yrjö Jahnsson foundation, Signe and Ane Gyllenberg foundation and Instrumentarium science foundation and TP by the HUCH research grant. The FinnGen project is funded by two grants from Business Finland (HUS 4685/31/2016 and UH 4386/31/2016) and the following industry partners: Abott, Astrazeneca UK, Biogen MA, Celgene Corporation, Celsegene International II Sar, Genentech, Merck Sharp & Dohme Corp, Pfizer, GloaxiSmithKline Intellectual Property Development, Sanofi US Services, Maze Therapeutics, Janssen Biotech. Following biobanks are acknowledged for the project samples: Auria Biobank (https://www.auria.fi/biopankki/en/), THL Biobank (https://thl.fi/en/web/thl-biobank), Helsinki Biobank (https://www.helsinki.biobankki.fi/en/home), Biobank of Northern Finland (https://www.pshp.fi/Tutkimus-ja-opetus/Biopankki/Pages/Biobank-Borealis-briefly-in-English.aspx), Finnish Clinical Biobank Tampere (https://www.tays.fi/en-US/Research_and_development/Finnish_Clinical_Biobank_Tampere), Biobank of Eastern Finland (https://ita-suomenbiopankki.fi/en/), Central Finland Biobank (https://www.kssp.fi/fl-Poliitilaale/Biopankki), Finnish Red Cross Blood Service Biobank (https://www.bloodservice.fi/Research_Projects/biobanking) and Terveystalo Biobank (https://www.terveystalo.com.fi/yritystietoa/Terveystalo-Biopankki/Biopankki/). All Finnish Biobanks are members of BBMRI and its infrastructure (http://www.bbmri.fi).

Competing interests None declared.

Patient consent for publication Obtained.


Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. The FinnGen individual level data may be accessed through applications to the Finnish Biobanks’ FinnBB portal, Fингенius (www.finnbb.fi). Summary data can be accessed through the FinnGen site https://www.finngen.fi/en/access_results.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non-Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/.

REFERENCES

## Contributors of FinnGen

### Steering Committee
- Aarno Palotie: Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland
- Mark Daly: Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland

### Pharmaceutical companies
- Howard Jacob: Abbvie, Chicago, IL, United States
- Athena Matakidou: Astra Zeneca, Cambridge, United Kingdom
- Heiko Runz: Biogen, Cambridge, MA, United States
- Sally John: Biogen, Cambridge, MA, United States
- Robert Plenge: Celgene, Summit, NJ, United States
- Mark McCarthy: Genentech, San Francisco, CA, United States
- Julie Hunkapiller Genentech, San Francisco, CA, United States
- Meg Ehm: GlaxoSmithKline, Brentford, United Kingdom
- Dawn Waterworth: GlaxoSmithKline, Brentford, United Kingdom
- Caroline Fox: Merck, Kenilworth, NJ, United States
- Anders Malarstig: Pfizer, New York, NY, United States
- Kathy Klinger: Sanofi, Paris, France
- Kathy Call: Sanofi, Paris, France

### University of Helsinki & Biobanks
- Tomi Mäkelä: HiLIFE, University of Helsinki, Finland
- Jaakko Kaprio: Institute for Molecular Medicine Finland, HiLIFE, Helsinki, Finland
- Petri Virolainen: Auria Biobank / Univ. of Turku / Hospital District of Southwest Finland, Turku, Finland
- Kari Pulkki: Auria Biobank / Univ. of Turku / Hospital District of Southwest Finland, Turku, Finland
- Terhi Kilpi: THL Biobank / Finnish Institute for Health and Welfare Helsinki, Finland
- Markus Perola: THL Biobank / Finnish Institute for Health and Welfare Helsinki, Finland
- Jukka Partanen: Finnish Red Cross Blood Service / Finnish Hematology Registry and Clinical Biobank, Helsinki, Finland
- Anne Pitkäranta: Hospital District of Helsinki and Uusimaa, Helsinki, Finland
- Riitta Kaarteenaho: Northern Finland Biobank Borealis / University of Oulu / Northern Ostrobothnia Hospital District, Oulu, Finland
- Seppo Vainio: Northern Finland Biobank Borealis / University of Oulu / Northern Ostrobothnia Hospital District, Oulu, Finland
- Kimmo Savinainen: Finnish Clinical Biobank Tampere / University of Tampere / Pirkanmaa Hospital District, Tampere, Finland
- Veli-Matti Kosma: Biobank of Eastern Finland / University of Eastern Finland / Northern Savo Hospital District, Kuopio, Finland
- Urho Kujala: Central Finland Biobank / University of Jyväskylä / Central Finland Health Care
Other Experts/ Non-Voting Members

Outi Tuovila  Business Finland, Helsinki, Finland
Minna Hendolin  Business Finland, Helsinki, Finland
Raimo Pakkamen  Business Finland, Helsinki, Finland

Scientific Committee

Pharmaceutical companies

Jeff Waring  Abbvie, Chicago, IL, United States
Bridget Riley-Gillis  Abbvie, Chicago, IL, United States
Athena Matakidou  Astra Zeneca, Cambridge, United Kingdom
Heiko Runz  Biogen, Cambridge, MA, United States
Jimmy Liu  Biogen, Cambridge, MA, United States
Shameek Biswas  Celgene, Summit, NJ, United States
Julie Hunkapiller  Genentech, San Francisco, CA, United States
Dawn Waterworth  GlaxoSmithKline, Brentford, United Kingdom
Meg Ehm  GlaxoSmithKline, Brentford, United Kingdom

Dorothee Diogo  Merck, Kenilworth, NJ, United States
Caroline Fox  Merck, Kenilworth, NJ, United States
Anders Malarstig  Pfizer, New York, NY, United States
Catherine Marshall  Pfizer, New York, NY, United States
Xinli Hu  Pfizer, New York, NY, United States
Kathy Call  Sanofi, Paris, France
Kathy Klinger  Sanofi, Paris, France
Matthias Gossel  Sanofi, Paris, France

University of Helsinki & Biobanks

Samuli Ripatti  Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Helsinki, Finland
Johanna Schleutker  Auria Biobank / Univ. of Turku / Hospital District of Southwest Finland, Turku, Finland
Markus Perola  THL Biobank / Finnish Institute for Health and Welfare Helsinki, Finland
Mikko Arvas  Finnish Red Cross Blood Service / Finnish Hematology Registry and Clinical Biobank, Helsinki, Finland
Olli Carpen  Hospital District of Helsinki and Uusimaa, Helsinki, Finland
Reetta Hinttala  Northern Finland Biobank Borealis / University of Oulu / Northern Ostrobothnia Hospital District, Oulu, Finland
Johannes Kettunen  Northern Finland Biobank Borealis / University of Oulu / Northern Ostrobothnia Hospital District, Oulu, Finland
Reijo Laaksonen  Finnish Clinical Biobank Tampere / University of Tampere / Pirkanmaa Hospital District, Tampere, Finland
Arto Mannermaa  Biobank of Eastern Finland / University of Eastern Finland / Northern Savo Hospital District, Kuopio, Finland
Juha Paloneva  Central Finland Biobank / University of Jyväskylä / Central Finland Health Care District, Jyväskylä, Finland
Urho Kujala  Central Finland Biobank / University of Jyväskylä / Central Finland Health Care District, Jyväskylä, Finland

Other Experts/ Non-Voting Members
Outi Tuovila  Business Finland, Helsinki, Finland
Minna Hendolin  Business Finland, Helsinki, Finland
Raimo Pakkanen  Business Finland, Helsinki, Finland

Clinical Groups
Neurology Group
Hilkka Soininen  Northern Savo Hospital District, Kuopio, Finland
Valtteri Julkunen  Northern Savo Hospital District, Kuopio, Finland
Anne Remes  Northern Ostrobothnia Hospital District, Oulu, Finland
Reetta Kälviäinen  Northern Savo Hospital District, Kuopio, Finland
Mikko Hiltunen  Northern Savo Hospital District, Kuopio, Finland
Jukka Peltola  Pirkanmaa Hospital District, Tampere, Finland
Pentti Tienari  Hospital District of Helsinki and Uusimaa, Helsinki, Finland
Juha Rinne  Hospital District of Southwest Finland, Turku, Finland
Adam Ziemann  Abbvie, Chicago, IL, United States
Jeffrey Waring  Abbvie, Chicago, IL, United States
Sahar Esmaeili  Abbvie, Chicago, IL, United States
Nizar Smaoui  Abbvie, Chicago, IL, United States
Anne Lehtonen  Abbvie, Chicago, IL, United States
Susan Eaton  Biogen, Cambridge, MA, United States
Heiko Runz  Biogen, Cambridge, MA, United States
Sanni Lahdenperä  Biogen, Cambridge, MA, United States
Shameek Biswas  Celgene, Summit, NJ, United States
John Michon  Genentech, San Francisco, CA, United States
Geoff Kerchner  Genentech, San Francisco, CA, United States
Julie Hunkapiller  Genentech, San Francisco, CA, United States
Natalie Bowers  Genentech, San Francisco, CA, United States
Edmond Teng  Genentech, San Francisco, CA, United States
John Eicher  Merck, Kenilworth, NJ, United States
Vinay Mehta  Merck, Kenilworth, NJ, United States
Padhraig Gormley  Merck, Kenilworth, NJ, United States
Kari Linden  Pfizer, New York, NY, United States
Christopher Whelan  Pfizer, New York, NY, United States
Fanli Xu  GlaxoSmithKline, Brentford, United Kingdom
David Pulford  GlaxoSmithKline, Brentford, United Kingdom

**Gastroenterology Group**

Martti Färkkilä  Hospital District of Helsinki and Uusimaa, Helsinki, Finland
Sampsu Pikkarainen  Hospital District of Helsinki and Uusimaa, Helsinki, Finland
Airi Jussila  Pirkanmaa Hospital District, Tampere, Finland
Timo Blomster  Northern Ostrobothnia Hospital District, Oulu, Finland
Mikko Kiviniemi  Northern Savo Hospital District, Kuopio, Finland
Markku Voutilainen  Hospital District of Southwest Finland, Turku, Finland
Bob Georgantas  Abbvie, Chicago, IL, United States
Graham Heap  Abbvie, Chicago, IL, United States
Jeffrey Waring  Abbvie, Chicago, IL, United States
Nizar Smaoui  Abbvie, Chicago, IL, United States
Fedik Rahimov  Abbvie, Chicago, IL, United States
Anne Lehtonen  Abbvie, Chicago, IL, United States
Keith Usiskin  Celgene, Summit, NJ, United States
Joseph Maranville  Celgene, Summit, NJ, United States
Tim Lu  Genentech, San Francisco, CA, United States
Natalie Bowers  Genentech, San Francisco, CA, United States
Danny Oh  Genentech, San Francisco, CA, United States
John Michon  Genentech, San Francisco, CA, United States
Vinay Mehta  Merck, Kenilworth, NJ, United States
Kirsu Kalpala  Pfizer, New York, NY, United States
Melissa Miller  Pfizer, New York, NY, United States
Xinli Hu  Pfizer, New York, NY, United States
Linda McCarthy  GlaxoSmithKline, Brentford, United Kingdom

**Rheumatology Group**

Kari Eklund  Hospital District of Helsinki and Uusimaa, Helsinki, Finland
Antti Palomäki  Hospital District of Southwest Finland, Turku, Finland
Pia Isomäki  Pirkanmaa Hospital District, Tampere, Finland
Laura Pirilä  Hospital District of Southwest Finland, Turku, Finland
Oili Kaipiainen-Seppänen  Northern Savo Hospital District, Kuopio, Finland
Johanna Huhtakangas  Northern Ostrobothnia Hospital District, Oulu, Finland
Bob Georgantas  Abbvie, Chicago, IL, United States
Jeffrey Waring  Abbvie, Chicago, IL, United States
Fedik Rahimov  Abbvie, Chicago, IL, United States
Apinya Lertratanakul  Abbvie, Chicago, IL, United States
Nizar Smaoui  Abbvie, Chicago, IL, United States
Anne Lehtonen  Abbvie, Chicago, IL, United States
David Close  Astra Zeneca, Cambridge, United Kingdom
Marla Hochfeld  Celgene, Summit, NJ, United States
Natalie Bowers  Genentech, San Francisco, CA, United States
John Michon  Genentech, San Francisco, CA, United States
Dorothee Diogo  Merck, Kenilworth, NJ, United States
Vinay Mehta  Merck, Kenilworth, NJ, United States
Kirsi Kalpala  Pfizer, New York, NY, United States
Nan Bing  Pfizer, New York, NY, United States
Xinli Hu  Pfizer, New York, NY, United States
Jorge Esparza Gordillo  GlaxoSmithKline, Brentford, United Kingdom
Nina Mars  Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Helsinki, Finland

Pulmonology Group
Tarja Laitinen  Pirkanmaa Hospital District, Tampere, Finland
Margit Pelkonen  Northern Savo Hospital District, Kuopio, Finland
Paula Kauppi  Hospital District of Helsinki and Uusimaa, Helsinki, Finland
Hannu Kankaanranta  Pirkanmaa Hospital District, Tampere, Finland
Terttu Harju  Northern Ostrobothnia Hospital District, Oulu, Finland
Nizar Smaoui  Abbvie, Chicago, IL, United States
David Close  Astra Zeneca, Cambridge, United Kingdom
Steven Greenberg  Celgene, Summit, NJ, United States
Hubert Chen  Genentech, San Francisco, CA, United States
Natalie Bowers  Genentech, San Francisco, CA, United States
John Michon  Genentech, San Francisco, CA, United States
Vinay Mehta  Merck, Kenilworth, NJ, United States
Jo Betts  GlaxoSmithKline, Brentford, United Kingdom
Soumitra Ghosh  GlaxoSmithKline, Brentford, United Kingdom

Cardiometabolic Diseases Group
Veikko Salomaa  Finnish Institute for Health and Welfare Helsinki, Finland
Teemu Niiranen  Finnish Institute for Health and Welfare Helsinki, Finland
Markus Juonala  Hospital District of Southwest Finland, Turku, Finland
Kaj Metsärinne  Hospital District of Southwest Finland, Turku, Finland
Mika Kähönen  Pirkanmaa Hospital District, Tampere, Finland
Juhani Juntila  Northern Ostrobothnia Hospital District, Oulu, Finland
Markku Laakso  Northern Savo Hospital District, Kuopio, Finland
Jussi Pihlajamäki  Northern Savo Hospital District, Kuopio, Finland
Juha Sinisalo  Hospital District of Helsinki and Uusimaa, Helsinki, Finland
Marja-Riitta Taskinen  Hospital District of Helsinki and Uusimaa, Helsinki, Finland
Tiinamaija Tuomi  Hospital District of Helsinki and Uusimaa, Helsinki, Finland
Jari Laukkanen  Central Finland Health Care District, Jyväskylä, Finland
Ben Challis  Astra Zeneca, Cambridge, United Kingdom
Andrew Peterson  Genentech, San Francisco, CA, United States
Julie Hunkapiller Genentech, San Francisco, CA, United States
Natalie Bowers Genentech, San Francisco, CA, United States
John Michon Genentech, San Francisco, CA, United States
Dorothee Diogo Merck, Kenilworth, NJ, United States
Audrey Chu Merck, Kenilworth, NJ, United States
Vinay Mehta Merck, Kenilworth, NJ, United States
Jaakko Parkkinen Pfizer, New York, NY, United States
Melissa Miller Pfizer, New York, NY, United States
Anthony Muslin Sanofi, Paris, France
Dawn Waterworth GlaxoSmithKline, Brentford, United Kingdom

Oncology Group
Heikki Joensuu Hospital District of Helsinki and Uusimaa, Helsinki, Finland
Tuomo Meretoja Hospital District of Helsinki and Uusimaa, Helsinki, Finland
Olli Carpen Hospital District of Helsinki and Uusimaa, Helsinki, Finland
Lauri Aaltonen Hospital District of Helsinki and Uusimaa, Helsinki, Finland
Annika Auronen Pirkanmaa Hospital District, Tampere, Finland
Peeter Karihtala Northern Ostrobothnia Hospital District, Oulu, Finland
Saila Kauppila Northern Ostrobothnia Hospital District, Oulu, Finland
Päivi Auvinen Northern Savo Hospital District, Kuopio, Finland
Klaus Elenius Hospital District of Southwest Finland, Turku, Finland
Relja Popovic Abbvie, Chicago, IL, United States
Jeffrey Waring Abbvie, Chicago, IL, United States
Bridget Riley-Gillis Abbvie, Chicago, IL, United States
Anne Lehtonen Abbvie, Chicago, IL, United States
Athena Matakidou Astra Zeneca, Cambridge, United Kingdom
Jennifer Schutzman Genentech, San Francisco, CA, United States
Julie Hunkapiller Genentech, San Francisco, CA, United States
Natalie Bowers Genentech, San Francisco, CA, United States
John Michon Genentech, San Francisco, CA, United States
Vinay Mehta Merck, Kenilworth, NJ, United States
Andrey Loboda Merck, Kenilworth, NJ, United States
Aparna Chhibber Merck, Kenilworth, NJ, United States
Heli Lehtonen Pfizer, New York, NY, United States
Stefan McDonough Pfizer, New York, NY, United States
Marika Crohns Sanofi, Paris, France
Diptee Kulkarni GlaxoSmithKline, Brentford, United Kingdom

Ophthalmology Group
Kai Kaarniranta Northern Savo Hospital District, Kuopio, Finland
Joni Turunen Hospital District of Helsinki and Uusimaa, Helsinki, Finland
Terhi Olliila Hospital District of Helsinki and Uusimaa, Helsinki, Finland
Sanna Seitsonen Hospital District of Helsinki and Uusimaa, Helsinki, Finland
Hannu Uusitalo  Pirkanmaa Hospital District, Tampere, Finland
Vesa Aaltonen  Hospital District of Southwest Finland, Turku, Finland
Hannele Uusitalo-Järvinen  Pirkanmaa Hospital District, Tampere, Finland
Marja Luodonpää  Northern Ostrobothnia Hospital District, Oulu, Finland
Nina Hautala  Northern Ostrobothnia Hospital District, Oulu, Finland
Heiko Runz  Biogen, Cambridge, MA, United States
Erich Strauss  Genentech, San Francisco, CA, United States
Natalie Bowers  Genentech, San Francisco, CA, United States
Hao Chen  Genentech, San Francisco, CA, United States
John Michon  Genentech, San Francisco, CA, United States
Anna Podgornaia  Merck, Kenilworth, NJ, United States
Vinay Mehta  Merck, Kenilworth, NJ, United States
Dorothee Diogo  Merck, Kenilworth, NJ, United States
Joshua Hoffman  GlaxoSmithKline, Brentford, United Kingdom

Dermatology Group
Kaisa Tasanen  Northern Ostrobothnia Hospital District, Oulu, Finland
Laura Huilaja  Northern Ostrobothnia Hospital District, Oulu, Finland
Katriina Hannula-Jouppi  Hospital District of Helsinki and Uusimaa, Helsinki, Finland
Tea Salmi  Pirkanmaa Hospital District, Tampere, Finland
Sirkku Peltonen  Hospital District of Southwest Finland, Turku, Finland
Leena Koulu  Hospital District of Southwest Finland, Turku, Finland
Ilkka Harvima  Northern Savo Hospital District, Kuopio, Finland
Kirsi Kalpala  Pfizer, New York, NY, United States
Ying Wu  Pfizer, New York, NY, United States
David Choy  Genentech, San Francisco, CA, United States
John Michon  Genentech, San Francisco, CA, United States
Nizar Smaoui  Abbvie, Chicago, IL, United States
Fedik Rahimov  Abbvie, Chicago, IL, United States
Anne Lehtonen  Abbvie, Chicago, IL, United States
Dawn Waterworth  GlaxoSmithKline, Brentford, United Kingdom

FinnGen Teams
Administration Team
Anu Jalanko  Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland
Risto Kajanne  Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland
Ulrike Lyhs  Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland
## Communication

Mari Kaunisto
Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland

## Analysis Team

<table>
<thead>
<tr>
<th>Name</th>
<th>Affiliation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Justin Wade Davis</td>
<td>Abbvie, Chicago, IL, United States</td>
</tr>
<tr>
<td>Bridget Riley-Gillis</td>
<td>Abbvie, Chicago, IL, United States</td>
</tr>
<tr>
<td>Danjuma Quarless</td>
<td>Abbvie, Chicago, IL, United States</td>
</tr>
<tr>
<td>Slavé Petrovski</td>
<td>Astra Zeneca, Cambridge, United Kingdom</td>
</tr>
<tr>
<td>Jimmy Liu</td>
<td>Biogen, Cambridge, MA, United States</td>
</tr>
<tr>
<td>Chia-Yen Chen</td>
<td>Biogen, Cambridge, MA, United States</td>
</tr>
<tr>
<td>Paola Bronson</td>
<td>Biogen, Cambridge, MA, United States</td>
</tr>
<tr>
<td>Robert Yang</td>
<td>Celgene, Summit, NJ, United States</td>
</tr>
<tr>
<td>Joseph Maranville</td>
<td>Celgene, Summit, NJ, United States</td>
</tr>
<tr>
<td>Shameek Biswas</td>
<td>Celgene, Summit, NJ, United States</td>
</tr>
<tr>
<td>Diana Chang</td>
<td>Genentech, San Francisco, CA, United States</td>
</tr>
<tr>
<td>Julie Hunkapiller</td>
<td>Genentech, San Francisco, CA, United States</td>
</tr>
<tr>
<td>Tushar Bhangale</td>
<td>Genentech, San Francisco, CA, United States</td>
</tr>
<tr>
<td>Natalie Bowers</td>
<td>Genentech, San Francisco, CA, United States</td>
</tr>
<tr>
<td>Dorothee Diogo</td>
<td>Merck, Kenilworth, NJ, United States</td>
</tr>
<tr>
<td>Emily Holzinger</td>
<td>Merck, Kenilworth, NJ, United States</td>
</tr>
<tr>
<td>Padhraig Gormley</td>
<td>Merck, Kenilworth, NJ, United States</td>
</tr>
<tr>
<td>Xulong Wang</td>
<td>Merck, Kenilworth, NJ, United States</td>
</tr>
<tr>
<td>Xing Chen</td>
<td>Pfizer, New York, NY, United States</td>
</tr>
<tr>
<td>Åsa Hedman</td>
<td>Pfizer, New York, NY, United States</td>
</tr>
<tr>
<td>Kirsi Auro</td>
<td>GlaxoSmithKline, Brentford, United Kingdom</td>
</tr>
<tr>
<td>Clarence Wang</td>
<td>Sanofi, Paris, France</td>
</tr>
<tr>
<td>Ethan Xu</td>
<td>Sanofi, Paris, France</td>
</tr>
<tr>
<td>Franck Auge</td>
<td>Sanofi, Paris, France</td>
</tr>
<tr>
<td>Clement Chatelain</td>
<td>Sanofi, Paris, France</td>
</tr>
<tr>
<td>Mitja Kurki</td>
<td>Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland / Broad Institute, Cambridge, MA, United States</td>
</tr>
<tr>
<td>Samuli Ripatti</td>
<td>Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland</td>
</tr>
<tr>
<td>Mark Daly</td>
<td>Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland</td>
</tr>
<tr>
<td>Juha Karjalainen</td>
<td>Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland / Broad Institute, Cambridge, MA, United States</td>
</tr>
<tr>
<td>Aki Havulinna</td>
<td>Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland</td>
</tr>
<tr>
<td>Anu Jalanko</td>
<td>Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland</td>
</tr>
<tr>
<td>Kimmo Palin</td>
<td>University of Helsinki, Helsinki, Finland</td>
</tr>
<tr>
<td>Priit Palta</td>
<td>Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland</td>
</tr>
<tr>
<td>Pietro Della Briotta Parolo</td>
<td>Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland</td>
</tr>
</tbody>
</table>

8
<table>
<thead>
<tr>
<th>Name</th>
<th>Institution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wei Zhou</td>
<td>Broad Institute, Cambridge, MA, United States</td>
</tr>
<tr>
<td>Susanna Lemmelä</td>
<td>Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland</td>
</tr>
<tr>
<td>Manuel Rivas</td>
<td>University of Stanford, Stanford, CA, United States</td>
</tr>
<tr>
<td>Jarmo Harju</td>
<td>Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland</td>
</tr>
<tr>
<td>Aarno Palotie</td>
<td>Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland</td>
</tr>
<tr>
<td>Arto Lehisto</td>
<td>Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland</td>
</tr>
<tr>
<td>Andrea Ganna</td>
<td>Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland</td>
</tr>
<tr>
<td>Vincent Llorens</td>
<td>Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland</td>
</tr>
<tr>
<td>Antti Karlsson</td>
<td>Auria Biobank / Univ. of Turku / Hospital District of Southwest Finland, Turku, Finland</td>
</tr>
<tr>
<td>Kati Kristiansson</td>
<td>THL Biobank / Finnish Institute for Health and Welfare Helsinki, Finland</td>
</tr>
<tr>
<td>Mikko Arvas</td>
<td>Finnish Red Cross Blood Service / Finnish Hematology Registry and Clinical Biobank, Helsinki, Finland</td>
</tr>
<tr>
<td>Kati Hyvärinen</td>
<td>Finnish Red Cross Blood Service / Finnish Hematology Registry and Clinical Biobank, Helsinki, Finland</td>
</tr>
<tr>
<td>Jarmo Ritari</td>
<td>Finnish Red Cross Blood Service / Finnish Hematology Registry and Clinical Biobank, Helsinki, Finland</td>
</tr>
<tr>
<td>Tiina Wahlfors</td>
<td>Finnish Red Cross Blood Service / Finnish Hematology Registry and Clinical Biobank, Helsinki, Finland</td>
</tr>
<tr>
<td>Miika Koskinen</td>
<td>Hospital District of Helsinki and Uusimaa, Helsinki, Finland BB/HUS/Univ Hosp Districts</td>
</tr>
<tr>
<td>Olli Carpen</td>
<td>Hospital District of Helsinki and Uusimaa, Helsinki, Finland BB/HUS/Univ Hosp Districts</td>
</tr>
<tr>
<td>Johannes Kettunen</td>
<td>Northern Finland Biobank Borealis / University of Oulu / Northern Ostrobothnia Hospital District, Oulu, Finland</td>
</tr>
<tr>
<td>Katri Pylkäs</td>
<td>Northern Finland Biobank Borealis / University of Oulu / Northern Ostrobothnia Hospital District, Oulu, Finland</td>
</tr>
<tr>
<td>Marita Kalaoja</td>
<td>Northern Finland Biobank Borealis / University of Oulu / Northern Ostrobothnia Hospital District, Oulu, Finland</td>
</tr>
<tr>
<td>Minna Karjalainen</td>
<td>Northern Finland Biobank Borealis / University of Oulu / Northern Ostrobothnia Hospital District, Oulu, Finland</td>
</tr>
<tr>
<td>Tuomo Mantere</td>
<td>Northern Finland Biobank Borealis / University of Oulu / Northern Ostrobothnia Hospital District, Oulu, Finland</td>
</tr>
<tr>
<td>Eeva Kangasniemi</td>
<td>Finnish Clinical Biobank Tampere / University of Tampere / Pirkanmaa Hospital District, Tampere, Finland</td>
</tr>
<tr>
<td>Sami Heikkinen</td>
<td>Biobank of Eastern Finland / University of Eastern Finland / Northern Savo Hospital District, Kuopio, Finland</td>
</tr>
<tr>
<td>Arto Mannermaa</td>
<td>Biobank of Eastern Finland / University of Eastern Finland / Northern Savo Hospital District, Kuopio, Finland</td>
</tr>
<tr>
<td>Eija Laakkonen</td>
<td>Central Finland Biobank / University of Jyväskylä / Central Finland Health Care District, Jyväskylä, Finland</td>
</tr>
<tr>
<td>Juha Kononen</td>
<td>Central Finland Biobank / University of Jyväskylä / Central Finland Health Care District, Jyväskylä, Finland</td>
</tr>
</tbody>
</table>
District, Jyväskylä, Finland

**Sample Collection Coordination**
- Anu Loukola  
  Hospital District of Helsinki and Uusimaa, Helsinki, Finland

**Sample Logistics**
- Päivi Laiho  
  THL Biobank / Finnish Institute for Health and Welfare Helsinki, Finland
- Tuuli Sistonen  
  THL Biobank / Finnish Institute for Health and Welfare Helsinki, Finland
- Essi Kaiharju  
  THL Biobank / Finnish Institute for Health and Welfare Helsinki, Finland
- Markku Laukkanen  
  THL Biobank / Finnish Institute for Health and Welfare Helsinki, Finland
- Elina Järvensivu  
  THL Biobank / Finnish Institute for Health and Welfare Helsinki, Finland
- Sini Lähteenmäki  
  THL Biobank / Finnish Institute for Health and Welfare Helsinki, Finland
- Lotta Männikkö  
  THL Biobank / Finnish Institute for Health and Welfare Helsinki, Finland
- Regis Wong  
  THL Biobank / Finnish Institute for Health and Welfare Helsinki, Finland

**Registry Data Operations**
- Kati Kristiansson  
  THL Biobank / Finnish Institute for Health and Welfare Helsinki, Finland
- Hannele Mattsson  
  THL Biobank / Finnish Institute for Health and Welfare Helsinki, Finland
- Susanna Lemmelä  
  Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland
- Tero Hiekkalinna  
  THL Biobank / Finnish Institute for Health and Welfare Helsinki, Finland
- Manuel González Jiménez  
  THL Biobank / Finnish Institute for Health and Welfare Helsinki, Finland

**Genotyping**
- Kati Donner  
  Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland

**Sequencing Informatics**
- Priit Palta  
  Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland
- Kalle Pärn  
  Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland
- Javier Nunez-Fontarnau  
  Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland

**Data Management and IT Infrastructure**
- Jarmo Harju  
  Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland
- Elina Kilpeläinen  
  Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland
- Timo P. Sipilä  
  Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland
- Georg Brein  
  Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland
- Alexander Dada  
  Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland
- Ghazal Awaisa  
  Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland
- Anastasia Sheherban  
  Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland
- Tuomas Sipilä  
  Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland
Clinical Endpoint Development
Hannele Laivuori   Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland
Aki Havulinna   Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland
Susanna Lemmelä   Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland
Tuomo Kiiskinen   Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland

Trajectory Team
Tarja Laitinen   Pirkanmaa Hospital District, Tampere, Finland
Harri Siirtola   University of Tampere, Tampere, Finland
Javier Gracia Tabuenca   University of Tampere, Tampere, Finland

Biobank Directors
Lila Kallio   Auria Biobank, Turku, Finland
Sirpa Soini   THL Biobank, Helsinki, Finland
Jukka Partanen   Blood Service Biobank, Helsinki, Finland
Kimmo Pitkänen   Helsinki Biobank, Helsinki, Finland
Seppo Vainio   Northern Finland Biobank Borealis, Oulu, Finland
Kimmo Savinainen   Tampere Biobank, Tampere, Finland
Veli-Matti Kosma   Biobank of Eastern Finland, Kuopio, Finland
Teijo Kuopio   Central Finland Biobank, Jyväskylä, Finland
Supplementary Table 1. The prospective epidemiological and disease-based cohorts, and hospital biobank samples in FinnGen Data Freeze 6

<table>
<thead>
<tr>
<th>Cohort</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Auria Biobank</td>
<td>29201</td>
</tr>
<tr>
<td>Biobank of Central Finland</td>
<td>7743</td>
</tr>
<tr>
<td>Biobank of Eastern Finland</td>
<td>7765</td>
</tr>
<tr>
<td>Blood Service Biobank</td>
<td>28901</td>
</tr>
<tr>
<td>Borealis Biobank</td>
<td>7390</td>
</tr>
<tr>
<td>Biobank Botnia</td>
<td>8681</td>
</tr>
<tr>
<td>Biobank Corogene</td>
<td>4689</td>
</tr>
<tr>
<td>Biobank FinHealth</td>
<td>5928</td>
</tr>
<tr>
<td>Helsinki Biobank</td>
<td>58693</td>
</tr>
<tr>
<td>Tampere Biobank</td>
<td>12394</td>
</tr>
<tr>
<td>Terveystalo Biobank</td>
<td>1709</td>
</tr>
<tr>
<td>THL Biobank ATBC</td>
<td>3836</td>
</tr>
<tr>
<td>THL Biobank FinIPF</td>
<td>201</td>
</tr>
<tr>
<td>THL Biobank FINRISK 1992</td>
<td>4931</td>
</tr>
<tr>
<td>THL Biobank FINRISK 1997</td>
<td>6997</td>
</tr>
<tr>
<td>THL Biobank FINRISK 2002</td>
<td>6869</td>
</tr>
<tr>
<td>THL Biobank FINRISK 2007</td>
<td>5143</td>
</tr>
<tr>
<td>THL Biobank FINRISK 2012</td>
<td>5233</td>
</tr>
<tr>
<td>THL Biobank GENERISK</td>
<td>6898</td>
</tr>
<tr>
<td>THL Biobank Health 2000</td>
<td>6529</td>
</tr>
<tr>
<td>THL Biobank Health 2011</td>
<td>708</td>
</tr>
<tr>
<td>THL Biobank HHS</td>
<td>2113</td>
</tr>
<tr>
<td>THL Biobank Kuusamo</td>
<td>123</td>
</tr>
<tr>
<td>THL Biobank Migraine</td>
<td>7717</td>
</tr>
<tr>
<td>THL Biobank SUPER</td>
<td>8466</td>
</tr>
<tr>
<td>THL Biobank Diabetes</td>
<td>10145</td>
</tr>
<tr>
<td>THL Biobank Twins</td>
<td>11402</td>
</tr>
<tr>
<td><strong>Total:</strong></td>
<td>260405</td>
</tr>
</tbody>
</table>

THL= Finnish Institute for Health and Welfare Helsinki, Finland
Supplementary Table 2. ICD-codes for OSA and comorbidities

<table>
<thead>
<tr>
<th>Comorbidity</th>
<th>ICD-10</th>
<th>ICD-9</th>
<th>ICD-8</th>
</tr>
</thead>
<tbody>
<tr>
<td>OSA</td>
<td>G47.3</td>
<td>3472</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>E10-E14</td>
<td>250</td>
<td>250</td>
</tr>
<tr>
<td>CHD</td>
<td>I20.0, I21, I22</td>
<td>410, 4110</td>
<td>410, 411.0</td>
</tr>
<tr>
<td>Asthma</td>
<td>J45, J46</td>
<td>493</td>
<td>493</td>
</tr>
<tr>
<td>COPD</td>
<td>J43, J44</td>
<td>492, 4912</td>
<td>492, 491.04</td>
</tr>
</tbody>
</table>

By combining codes from different registries, we generate phenotype endpoints. Finnish national version for each International Statistical Classification of Diseases (ICD)-codes were used. These ICD-code criteria are all regular expressions for a hierarchical search. OSA=obstructive sleep apnoea, CHD=coronary heart disease.