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=5.13×10^{-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% CI 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.

Key messages
- Is obstructive sleep apnoea (OSA) an independent risk factor for severe COVID-19?
- Patients with OSA have a higher risk to be hospitalised when affected by COVID-19 than non-OSA individuals.
- 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 and patients with OSA with suspected or confirmed COVID-19 infection should be monitored closely.

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.1,3 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-19.1,2,7,9,12 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 sometime 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.13 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.\textsuperscript{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-Hypopnoea 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\textsuperscript{2-9} concerning the role of OSA on COVID-19 hospitalisation.

**Statistical methods**

Differences in baseline demographics and clinical characteristics were tested using \( \chi^2 \) 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 aforementioned tests are Bonferroni corrected. Logistic regression was used to calculate OR between hospitalised and non-hospitalised groups. Model 1 was adjusted for age and 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.

**Table 1** Comparison of the baseline characteristics among COVID-19 positive individuals

<table>
<thead>
<tr>
<th></th>
<th>All n=445</th>
<th>Non-hospitalised n=354</th>
<th>Hospitalised n=91</th>
<th>( P ) unadjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean in years, SD)</td>
<td>52.7 (17.4)</td>
<td>49.3 (16.3)</td>
<td>65.9 (14.8)</td>
<td>1.06×10(^{-15} )</td>
</tr>
<tr>
<td>Sex (male) (N, %)</td>
<td>166 (37.3)</td>
<td>133 (37.6)</td>
<td>33 (36.3)</td>
<td>1</td>
</tr>
<tr>
<td>OSA (N, %)</td>
<td>38 (8.5)</td>
<td>19 (5.4)</td>
<td>19 (20.9)</td>
<td>5.13×10(^{-5} )</td>
</tr>
<tr>
<td>BMI (mean kg/m(^2), SD)</td>
<td>27.13 (5.44)</td>
<td>26.54 (5.20)</td>
<td>29.25 (5.78)</td>
<td>0.014*</td>
</tr>
<tr>
<td>Hypertension (N, %)</td>
<td>79 (17.8)</td>
<td>40 (11.3)</td>
<td>39 (42.9)</td>
<td>5.03×10(^{-11} )</td>
</tr>
<tr>
<td>Diabetes (N, %)</td>
<td>46 (10.3)</td>
<td>23 (6.5)</td>
<td>23 (25.3)</td>
<td>3.45×10(^{-6} )</td>
</tr>
<tr>
<td>CHD (N, %)</td>
<td>21 (4.7)</td>
<td>9 (2.5)</td>
<td>12 (13.2)</td>
<td>5.20×10(^{-4} )</td>
</tr>
<tr>
<td>Asthma/COPD</td>
<td>54 (12.1)</td>
<td>40 (11.3)</td>
<td>14 (15.4)</td>
<td>1</td>
</tr>
</tbody>
</table>

Differences and associations between non-hospitalised and hospitalised COVID-19 positive individuals. Baseline demographics and clinical characteristics \( P \) 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 (table 3) and similarly between COVID-19-positive and non-COVID-19 groups.

Our results and previous findings from the corresponding studies2–9 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 patients with OSA.

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%.18 Ninety-one (20.4%) patients required hospitalisation (36.3% male, mean age 65.9 years) including 19 patients with OSA (table 1).

Prevalence of OSA (p=5.13×10−5), hypertension (p=5.03×10−4), diabetes (p=3.45×10−5) 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=1.06×10−3, 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=1.74×10−3) and they faced hospitalisation more often (p=3.21×10−3). 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>Description</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>Age (mean in years, SD)</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>Sex (male) (N, %)</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>BMI (mean kg/m^2, SD)</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>Comorbidities or outcomes (N, %)</td>
<td>118 (29.0)</td>
<td>24 (63.2)</td>
<td>1.74×10−4</td>
<td>12 (63.2)</td>
<td>12 (63.2)</td>
<td>1</td>
</tr>
<tr>
<td>Hospitalised (N, %)</td>
<td>72 (17.7)</td>
<td>19 (50.0)</td>
<td>3.21×10−5</td>
<td>12 (63.2)</td>
<td>12 (63.2)</td>
<td>1</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.
other comorbidities in addition to OSA (62.8 years, 68.9 years, p=0.72, 30.26 kg/m², 32.67 kg/m², p=1.00, respectively). Time since the first diagnosis of OSA to COVID-19 infection was not significantly different between non-hospitalised and hospitalised groups (6.6 years, 8.6 years, p=0.37, respectively).

We tested if OSA is associated with the risk of severe COVID-19 infection, determined as being hospitalised (n=91), or COVID-19 infection in general (n=145). While OSA did not affect the risk of contracting COVID-19 (p=0.25), patients with OSA had a considerably elevated risk for being hospitalised due to severe COVID-19 (OR=2.93 (95% CI 1.02 to 8.39), p=0.045, adjusted for age, sex, BMI, hypertension, diabetes, CHD, asthma and COPD; table 3).

We performed a meta-analysis by pooling the comparable endpoints between the published studies7-9 and examined the association with severe COVID-19 with and without adjusting for BMI. The studies, including our study, consisted of 15 835 COVID-19 positive individuals including 1294 patients with OSA. Overall, we observed over twofold increase in the pooled estimate prior to including 1294 patients with OSA. Overall, we observed study without adjusting for BMI. The studies, including our study, 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.

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

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

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 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).
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.1–3 However, only one study showed a statistically significant association between OSA and severe COVID-19 after adjusting for BMI.3 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-19.10 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
1Institute for Molecular Medicine Finland (FIMM), University of Helsinki, Helsinki, Finland
2Orthodontics, Department of Oral and Maxillofacial Diseases, Clinicum, Faculty of Medicine, University of Helsinki, Helsinki, Finland
3Department of Oral and Maxillofacial Diseases, Helsinki University Hospital (HUH), Helsinki, Finland
4Finnish Institute for Health and Welfare, Helsinki, Finland
5Broad Institute of MIT and Harvard, Cambridge, MA, USA
6Sleep Unit, Heart and Lung Center, Helsinki University Hospital (HUH), Helsinki, Finland
7Analytic and Translational Genetics Unit (ATGU), Department of Medicine, Department of Neurology and Department of Psychiatry, Massachusetts General Hospital, Boston, Massachusetts, USA
8Department of Public Health, University of Helsinki, Helsinki, Finland
9Stanford 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, SHu, 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 Junellus Foundation and University of Helsinki HILIFE 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 Junellus 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: Abbvie, AstraZeneca UK, Biogen MA, Celgene Corporation, Celgene International II Sàrl, Genentech, Merck Sharp & Dohme Corp, Pfizer, GlaxoSmithKline 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.helsinginbiopankki.fi/en/home), Biobank Borealis 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.kjsp.fi-fi/Potilaatte/Biopankki), Finnish Red Cross Blood Service Biobank (https://www.bloodservice.fi/Research_Projects/biobanking) and Terveytestalo Biobank (https://www.terveytestalo.fi/fi/Vrystytteloa/Terveytestalo-Biopankki/Biopankki/). All Finnish Biobanks are members of BMBMI infrastructure (http://www.bmbmi.fi).

Competing interests  
None declared.

Patient consent for publication  
Obtained.

Ethics approval  

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, Fingeneous (www.finbb.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

<table>
<thead>
<tr>
<th>Name</th>
<th>Affiliation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outi Tuovila</td>
<td>Business Finland, Helsinki, Finland</td>
</tr>
<tr>
<td>Minna Hendolin</td>
<td>Business Finland, Helsinki, Finland</td>
</tr>
<tr>
<td>Raimo Pakkamen</td>
<td>Business Finland, Helsinki, Finland</td>
</tr>
</tbody>
</table>

Scientific Committee

Pharmaceutical companies

<table>
<thead>
<tr>
<th>Name</th>
<th>Affiliation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jeff Waring</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>Athena Matakidou</td>
<td>Astra Zeneca, Cambridge, United Kingdom</td>
</tr>
<tr>
<td>Heiko Runz</td>
<td>Biogen, Cambridge, MA, United States</td>
</tr>
<tr>
<td>Jimmy Liu</td>
<td>Biogen, Cambridge, MA, United States</td>
</tr>
<tr>
<td>Shameek Biswas</td>
<td>Celgene, Summit, NJ, United States</td>
</tr>
<tr>
<td>Julie Hunkapiller</td>
<td>Genentech, San Francisco, CA, United States</td>
</tr>
<tr>
<td>Dawn Waterworth</td>
<td>GlaxoSmithKline, Brentford, United Kingdom</td>
</tr>
<tr>
<td>Meg Ehm</td>
<td>GlaxoSmithKline, Brentford, United Kingdom</td>
</tr>
<tr>
<td>Dorothee Diogo</td>
<td>Merck, Kenilworth, NJ, United States</td>
</tr>
<tr>
<td>Caroline Fox</td>
<td>Merck, Kenilworth, NJ, United States</td>
</tr>
<tr>
<td>Anders Malarstig</td>
<td>Pfizer, New York, NY, United States</td>
</tr>
<tr>
<td>Catherine Marshall</td>
<td>Pfizer, New York, NY, United States</td>
</tr>
<tr>
<td>Xinli Hu</td>
<td>Pfizer, New York, NY, United States</td>
</tr>
<tr>
<td>Kathy Call</td>
<td>Sanofi, Paris, France</td>
</tr>
<tr>
<td>Kathy Klinger</td>
<td>Sanofi, Paris, France</td>
</tr>
<tr>
<td>Matthias Gossel</td>
<td>Sanofi, Paris, France</td>
</tr>
</tbody>
</table>

University of Helsinki & Biobanks

<table>
<thead>
<tr>
<th>Name</th>
<th>Affiliation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Samuli Ripatti</td>
<td>Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki,</td>
</tr>
<tr>
<td>Helsinki, Finland</td>
<td></td>
</tr>
<tr>
<td>Johanna Schleutker</td>
<td>Auria Biobank / Univ. of Turku / Hospital District of Southwest Finland, Turku, Finland</td>
</tr>
<tr>
<td>Markus Perola</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>Olli Carpen</td>
<td>Hospital District of Helsinki and Uusimaa, Helsinki, Finland</td>
</tr>
<tr>
<td>Reetta Hinttala</td>
<td>Northern Finland Biobank Borealis / University of Oulu / Northern Ostrobothnia Hospital District, Oulu, Finland</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>Reijo Laaksonen</td>
<td>Finnish Clinical Biobank Tampere / University of Tampere / Pirkanmaa Hospital District, Tampere, Finland</td>
</tr>
</tbody>
</table>
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 Esmaeeli | 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

Kirsti 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

---

<table>
<thead>
<tr>
<th>Name</th>
<th>Institution and Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Natalie Bowers</td>
<td>Genentech, San Francisco, CA, United States</td>
</tr>
<tr>
<td>John Michon</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>Vinay Mehta</td>
<td>Merck, Kenilworth, NJ, United States</td>
</tr>
<tr>
<td>Kirsii Kalpala</td>
<td>Pfizer, New York, NY, United States</td>
</tr>
<tr>
<td>Nan Bing</td>
<td>Pfizer, New York, NY, United States</td>
</tr>
<tr>
<td>Xinli Hu</td>
<td>Pfizer, New York, NY, United States</td>
</tr>
<tr>
<td>Jorge Esparza Gordillo</td>
<td>GlaxoSmithKline, Brentford, United Kingdom</td>
</tr>
<tr>
<td>Nina Mars</td>
<td>Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Helsinki, Finland</td>
</tr>
<tr>
<td>Margit Pelkonen</td>
<td>Northern Savo Hospital District, Kuopio, Finland</td>
</tr>
<tr>
<td>Paula Kauppi</td>
<td>Hospital District of Helsinki and Uusimaa, Helsinki, Finland</td>
</tr>
<tr>
<td>Hannu Kankaanranta</td>
<td>Pirkanmaa Hospital District, Tampere, Finland</td>
</tr>
<tr>
<td>Terttu Harju</td>
<td>Northern Ostrobothnia Hospital District, Oulu, Finland</td>
</tr>
<tr>
<td>Nizar Smaoui</td>
<td>Abbvie, Chicago, IL, United States</td>
</tr>
<tr>
<td>David Close</td>
<td>Astra Zeneca, Cambridge, United Kingdom</td>
</tr>
<tr>
<td>Steven Greenberg</td>
<td>Genentech, San Francisco, CA, United States</td>
</tr>
<tr>
<td>Hubert Chen</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>John Michon</td>
<td>Genentech, San Francisco, CA, United States</td>
</tr>
<tr>
<td>Jo Betts</td>
<td>GlaxoSmithKline, Brentford, United Kingdom</td>
</tr>
<tr>
<td>Soumitra Ghosh</td>
<td>GlaxoSmithKline, Brentford, United Kingdom</td>
</tr>
<tr>
<td>Veikko Salomaa</td>
<td>Finnish Institute for Health and Welfare Helsinki, Finland</td>
</tr>
<tr>
<td>Teemu Niiranen</td>
<td>Finnish Institute for Health and Welfare Helsinki, Finland</td>
</tr>
<tr>
<td>Markus Juonala</td>
<td>Hospital District of Southwest Finland, Turku, Finland</td>
</tr>
<tr>
<td>Kaj Metsärinne</td>
<td>Hospital District of Southwest Finland, Turku, Finland</td>
</tr>
<tr>
<td>Mika Kähönen</td>
<td>Pirkanmaa Hospital District, Tampere, Finland</td>
</tr>
<tr>
<td>Juhani Junnila</td>
<td>Northern Ostrobothnia Hospital District, Oulu, Finland</td>
</tr>
<tr>
<td>Markku Laakso</td>
<td>Northern Savo Hospital District, Kuopio, Finland</td>
</tr>
<tr>
<td>Jussi Pihljamäki</td>
<td>Northern Savo Hospital District, Kuopio, Finland</td>
</tr>
<tr>
<td>Juha Sinisalo</td>
<td>Hospital District of Helsinki and Uusimaa, Helsinki, Finland</td>
</tr>
<tr>
<td>Marja-Riitta Taskinen</td>
<td>Hospital District of Helsinki and Uusimaa, Helsinki, Finland</td>
</tr>
<tr>
<td>Tiinamaaja Tuomi</td>
<td>Hospital District of Helsinki and Uusimaa, Helsinki, Finland</td>
</tr>
<tr>
<td>Jari Laukkanen</td>
<td>Central Finland Health Care District, Jyväskylä, Finland</td>
</tr>
<tr>
<td>Ben Challis</td>
<td>Astra Zeneca, Cambridge, United Kingdom</td>
</tr>
<tr>
<td>Andrew Peterson</td>
<td>Genentech, San Francisco, CA, United States</td>
</tr>
</tbody>
</table>
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
Paivi 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 Ollila Hospital District of Helsinki and Uusimaa, Helsinki, Finland
Sanna Seitsonen Hospital District of Helsinki and Uusimaa, Helsinki, Finland
<table>
<thead>
<tr>
<th>Name</th>
<th>Affiliation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hannu Uusitalo</td>
<td>Pirkanmaa Hospital District, Tampere, Finland</td>
</tr>
<tr>
<td>Vesa Aaltoinen</td>
<td>Hospital District of Southwest Finland, Turku, Finland</td>
</tr>
<tr>
<td>Hannele Uusitalo-Järvinen</td>
<td>Pirkanmaa Hospital District, Tampere, Finland</td>
</tr>
<tr>
<td>Marja Luodonpää</td>
<td>Northern Ostrobothnia Hospital District, Oulu, Finland</td>
</tr>
<tr>
<td>Nina Hautala</td>
<td>Northern Ostrobothnia Hospital District, Oulu, Finland</td>
</tr>
<tr>
<td>Heiko Runz</td>
<td>Biogen, Cambridge, MA, United States</td>
</tr>
<tr>
<td>Erich Strauss</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>Hao Chen</td>
<td>Genentech, San Francisco, CA, United States</td>
</tr>
<tr>
<td>John Michon</td>
<td>Genentech, San Francisco, CA, United States</td>
</tr>
<tr>
<td>Anna Podgornaia</td>
<td>Merck, Kenilworth, NJ, United States</td>
</tr>
<tr>
<td>Vinay Mehta</td>
<td>Merck, Kenilworth, NJ, United States</td>
</tr>
<tr>
<td>Dorothée Diogo</td>
<td>Merck, Kenilworth, NJ, United States</td>
</tr>
<tr>
<td>Joshua Hoffman</td>
<td>GlaxoSmithKline, Brentford, United Kingdom</td>
</tr>
</tbody>
</table>

**Dermatology Group**

<table>
<thead>
<tr>
<th>Name</th>
<th>Affiliation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kaisa Tasanen</td>
<td>Northern Ostrobothnia Hospital District, Oulu, Finland</td>
</tr>
<tr>
<td>Laura Huilaja</td>
<td>Northern Ostrobothnia Hospital District, Oulu, Finland</td>
</tr>
<tr>
<td>Katiirina Hannula-Jouppi</td>
<td>Hospital District of Helsinki and Uusimaa, Helsinki, Finland</td>
</tr>
<tr>
<td>Teeta Salmi</td>
<td>Pirkanmaa Hospital District, Tampere, Finland</td>
</tr>
<tr>
<td>Sirkku Peltonen</td>
<td>Hospital District of Southwest Finland, Turku, Finland</td>
</tr>
<tr>
<td>Leena Koulu</td>
<td>Hospital District of Southwest Finland, Turku, Finland</td>
</tr>
<tr>
<td>Ilkka Harvina</td>
<td>Northern Savo Hospital District, Kuopio, Finland</td>
</tr>
<tr>
<td>Kirsi Kalpala</td>
<td>Pfizer, New York, NY, United States</td>
</tr>
<tr>
<td>Ying Wu</td>
<td>Pfizer, New York, NY, United States</td>
</tr>
<tr>
<td>David Choy</td>
<td>Genentech, San Francisco, CA, United States</td>
</tr>
<tr>
<td>John Michon</td>
<td>Genentech, San Francisco, CA, United States</td>
</tr>
<tr>
<td>Nizar Smaoui</td>
<td>Abbvie, Chicago, IL, United States</td>
</tr>
<tr>
<td>Fedik Rahimov</td>
<td>Abbvie, Chicago, IL, United States</td>
</tr>
<tr>
<td>Anne Lehtonen</td>
<td>Abbvie, Chicago, IL, United States</td>
</tr>
<tr>
<td>Dawn Waterworth</td>
<td>GlaxoSmithKline, Brentford, United Kingdom</td>
</tr>
</tbody>
</table>

**FinnGen Teams**

**Administration Team**

<table>
<thead>
<tr>
<th>Name</th>
<th>Affiliation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anu Jalanko</td>
<td>Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland</td>
</tr>
<tr>
<td>Risto Kajanne</td>
<td>Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland</td>
</tr>
<tr>
<td>Ulrike Lyhs</td>
<td>Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland</td>
</tr>
</tbody>
</table>
Communication
Mari Kaunisto  Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland

Analysis Team
Justin Wade Davis  Abbvie, Chicago, IL, United States
Bridget Riley-Gillis  Abbvie, Chicago, IL, United States
Danjuma Quarless  Abbvie, Chicago, IL, United States
Slavé Petrovski  Astra Zeneca, Cambridge, United Kingdom
Jimmy Liu  Biogen, Cambridge, MA, United States
Chia-Yen Chen  Biogen, Cambridge, MA, United States
Paola Bronson  Biogen, Cambridge, MA, United States
Robert Yang  Celgene, Summit, NJ, United States
Joseph Maranville  Celgene, Summit, NJ, United States
Shameek Biswas  Celgene, Summit, NJ, United States
Diana Chang  Genentech, San Francisco, CA, United States
Julie Hunkapiller  Genentech, San Francisco, CA, United States
Tushar Bhangale  Genentech, San Francisco, CA, United States
Natalie Bowers  Genentech, San Francisco, CA, United States
Dorothee Diogo  Merck, Kenilworth, NJ, United States
Emily Holzinger  Merck, Kenilworth, NJ, United States
Padhraig Gormley  Merck, Kenilworth, NJ, United States
Xulong Wang  Merck, Kenilworth, NJ, United States
Xing Chen  Pfizer, New York, NY, United States
Åsa Hedman  Pfizer, New York, NY, United States
Kirsi Auro  GlaxoSmithKline, Brentford, United Kingdom
Clarence Wang  Sanofi, Paris, France
Ethan Xu  Sanofi, Paris, France
Franck Auge  Sanofi, Paris, France
Clement Chatelain  Sanofi, Paris, France
Mitja Kurki  Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland / Broad Institute, Cambridge, MA, United States
Samuli Ripatti  Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland
Mark Daly  Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland
Juha Karjalainen  Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland / Broad Institute, Cambridge, MA, United States
Aki Havulinna  Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland
Anu Jalanko  Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland
Kimmo Palin  University of Helsinki, Helsinki, Finland
Priit Palta  Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland
Pietro Della Briotta Parolo  Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland
Wei Zhou  Broad Institute, Cambridge, MA, United States
Susanna Lemmelä  Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland
Manuel Rivas  University of Stanford, Stanford, CA, United States
Jarmo Harju  Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland
Aarno Palotie  Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland
Arto Lehisto  Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland
Andrea Ganna  Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland
Vincent Llorens  Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland
Antti Karlsson  Auria Biobank / Univ. of Turku / Hospital District of Southwest Finland, Turku, Finland
Kati Kristiansson  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
Kati Hyvärinen  Finnish Red Cross Blood Service / Finnish Hematology Registry and Clinical Biobank, Helsinki, Finland
Jarmo Ritari  Finnish Red Cross Blood Service / Finnish Hematology Registry and Clinical Biobank, Helsinki, Finland
Tiina Wahlfors  Finnish Red Cross Blood Service / Finnish Hematology Registry and Clinical Biobank, Helsinki, Finland
Miika Koskinen  Hospital District of Helsinki and Uusimaa, Helsinki, Finland BB/HUS/Univ Hosp Districts
Olli Carpen  Hospital District of Helsinki and Uusimaa, Helsinki, Finland BB/HUS/Univ Hosp Districts
Johannes Kettunen  Northern Finland Biobank Borealis / University of Oulu / Northern Ostrobothnia Hospital District, Oulu, Finland
Katri Pylkäs  Northern Finland Biobank Borealis / University of Oulu / Northern Ostrobothnia Hospital District, Oulu, Finland
Marita Kalaoja  Northern Finland Biobank Borealis / University of Oulu / Northern Ostrobothnia Hospital District, Oulu, Finland
Minna Karjalainen  Northern Finland Biobank Borealis / University of Oulu / Northern Ostrobothnia Hospital District, Oulu, Finland
Tuomo Mantere  Northern Finland Biobank Borealis / University of Oulu / Northern Ostrobothnia Hospital District, Oulu, Finland
Eeva Kangasniemi  Finnish Clinical Biobank Tampere / University of Tampere / Pirkanmaa Hospital District, Tampere, Finland
Sami Heikkinen  Biobank of Eastern Finland / University of Eastern Finland / Northern Savo Hospital District, Kuopio, Finland
Arto Mannermaa  Biobank of Eastern Finland / University of Eastern Finland / Northern Savo Hospital District, Kuopio, Finland
Eija Laakkonen  Central Finland Biobank / University of Jyväskylä / Central Finland Health Care District, Jyväskylä, Finland
Juha Kononen  Central Finland Biobank / University of Jyväskylä / Central Finland Health Care District, Jyväskylä, Finland
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>TRL Biobank ATBC</td>
<td>3836</td>
</tr>
<tr>
<td>TRL Biobank FinPF</td>
<td>201</td>
</tr>
<tr>
<td>TRL Biobank FINRISK 1992</td>
<td>4931</td>
</tr>
<tr>
<td>TRL Biobank FINRISK 1997</td>
<td>6997</td>
</tr>
<tr>
<td>TRL Biobank FINRISK 2002</td>
<td>6869</td>
</tr>
<tr>
<td>TRL Biobank FINRISK 2007</td>
<td>5143</td>
</tr>
<tr>
<td>TRL Biobank FINRISK 2012</td>
<td>5233</td>
</tr>
<tr>
<td>TRL Biobank GENERISK</td>
<td>6898</td>
</tr>
<tr>
<td>TRL Biobank Health 2000</td>
<td>6529</td>
</tr>
<tr>
<td>TRL Biobank Health 2011</td>
<td>708</td>
</tr>
<tr>
<td>TRL Biobank HHS</td>
<td>2113</td>
</tr>
<tr>
<td>TRL Biobank Kuusamo</td>
<td>123</td>
</tr>
<tr>
<td>TRL Biobank Migraine</td>
<td>7717</td>
</tr>
<tr>
<td>TRL Biobank SUPER</td>
<td>8466</td>
</tr>
<tr>
<td>TRL Biobank Diabetes</td>
<td>10145</td>
</tr>
<tr>
<td>TRL 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></th>
<th>ICD-10</th>
<th>ICD-9</th>
<th>ICD-8</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>OSA</strong></td>
<td>G47.3</td>
<td>3472</td>
<td></td>
</tr>
<tr>
<td><strong>DIABETES</strong></td>
<td>E10-E14</td>
<td>250</td>
<td>250</td>
</tr>
<tr>
<td><strong>CHD</strong></td>
<td>I20.0, I21, I22</td>
<td>410, 4110</td>
<td>410, 411.0</td>
</tr>
<tr>
<td><strong>ASTHMA</strong></td>
<td>J45, J46</td>
<td>493</td>
<td>493</td>
</tr>
<tr>
<td><strong>COPD</strong></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.