Comprehensive Inherited Risk Estimation for Risk-Based Breast Cancer Screening in Women

Nina Mars, MD, PhD[1,2]; Sini Kerminen, PhD[1]; Max Tamlander, MD[1]; Matti Pirinen, PhD[1,3,4]; Eveliina Jakkula, MD, PhD[5,6]; Kirsimari Aaltonen, MD, PhD[5,6]; Tuomo Meretoja, MD, PhD[7,8]; Sirpa Heinävaara, PhD[4,9]; Elisabeth Widén, MD, PhD[1]; and Samuli Ripatti, PhD[1,2,4]; on behalf of FinnGen

DOI https://doi.org/10.1200/JCO.23.00295

ABSTRACT

PURPOSE Family history (FH) and pathogenic variants (PVs) are used for guiding risk surveillance in selected high-risk women but little is known about their impact for breast cancer screening on population level. In addition, polygenic risk scores (PRSs) have been shown to efficiently stratify breast cancer risk through combining information about common genetic factors into one measure.

METHODS In longitudinal real-life data, we evaluate PRS, FH, and PVs for stratified screening. Using FinnGen (N = 117,252), linked to the Mass Screening Registry for breast cancer (1992-2019; nationwide organized biennial screening for age 50-69 years), we assessed the screening performance of a breast cancer PRS and compared its performance with FH of breast cancer and PVs in moderate- (*CHEK2*)- to high-risk (*PALB2*) susceptibility genes.

RESULTS Effect sizes for FH, PVs, and high PRS (>90th percentile) were comparable in screening-aged women, with similar implications for shifting age at screening onset. A high PRS identified women more likely to be diagnosed with breast cancer after a positive screening finding (positive predictive value [PPV], 39.5% [95% CI, 37.6 to 41.5]). Combinations of risk factors increased the PPVs up to 45% to 50%. A high PRS conferred an elevated risk of interval breast cancer (hazard ratio [HR], 2.78 [95% CI, 2.00 to 3.86] at age 50 years; HR, 2.48 [95% CI, 1.67 to 3.70] at age 60 years), and women with a low PRS (<10th percentile) had a low risk for both interval- and screen-detected breast cancers.

CONCLUSION Using real-life screening data, this study demonstrates the effectiveness of a breast cancer PRS for risk stratification, alone and combined with FH and PVs. Further research is required to evaluate their impact in a prospective risk-stratified screening program, including cost-effectiveness.

ACCOMPANYING CONTENT

Editorial, p. 1462

Appendix

Data Supplement

Accepted December 20, 2023
Published February 29, 2024

J Clin Oncol 42:1477-1487

View Online Article

INTRODUCTION

Organized population-based screening has a prominent role in early detection of breast cancer in many countries, and reduction of breast cancer mortality has followed adoption of such screening programmes.[1,2] Yet, the programs have also generated much controversy around the balance of benefits and harms, particularly regarding the age of initiation and screening interval. Instead of the one-size-fits-all regimen, increasing evidence suggests that cost-efficiency and the benefit-harm balance could be improved by risk-tailored screening, giving the opportunity to personalize the start and stop ages, and the screening interval.[3] Such risk-tailored surveillance has long been used for specific subgroups, such as carriers of pathogenic variants (PVs) in moderate- or high-risk breast cancer susceptibility genes (eg, *BRCA1* and *PALB2*), and with accumulation of early-onset breast cancer in the family.[4,5]

In addition to moderate- and high-risk variants in susceptibility genes, breast cancer has a polygenic inheritance where many common variants across the genome jointly contribute to disease risk. Polygenic risk scores (PRS) combine such information into a single metric of inherited disease susceptibility.[6] Compared with individuals with an average breast cancer PRS, a high PRS confers an up to three- to five-fold risk increase to breast cancer, with a lifetime risk of over 30%.[7,8] The breast cancer PRS also considerably modifies the risk conferred by moderate- and high-risk variants.[9,10] Previous studies show that breast cancer PRS offers opportunities for risk-tailored surveillance,[7,8] but there is limited evidence on impact of PRSs for identifying high-risk women for stratified screening on the basis of population-based screening data.

In Finland, biennial screening is offered free for all women between age 50 and 69 years through a nationwide screening

CONTEXT

Key Objective

The current approach to population breast cancer screening uses a one-size-fits-all regimen, yet studies on inherited risk factors, including polygenic risk scores (PRS) for breast cancer, family history, and pathogenic variants (PVs) in susceptibility genes, suggest the potential for personalized screening on the basis of individual risk profiles. How do such inherited risk factors, particularly the PRS, which is a more recently identified risk factor, perform in real-life screening data?

Knowledge Generated

The breast cancer PRS served for risk stratification of breast cancer screening both alone and combined with FH and PVs. A high PRS correlated with a high positive predictive value for breast cancer screening and conferred an elevated risk for interval breast cancer.

Relevance *(G. Fleming)*

Future trials attempting to personalize type and schedule of breast cancer screening should strongly consider incorporation of a PRS along with other risk factors.*

*Relevance section written by *JCO* Associate Editor Gini Fleming, MD.

program. We estimate the impact of PRS in this screening setting, comparing the effect of PRS in risk stratification to family history (FH) and known moderate- to high-risk PVs in breast cancer susceptibility genes. FinnGen combines genomewide genotyping to nationwide health registries, including the Mass Screening Registry, allowing assessment of PRS in the breast cancer screening context starting from the initiation of a nationwide breast cancer screening program in 1992.[11]

METHODS

Patients and Outcomes

The FinnGen study, a collection of Finnish prospective epidemiologic cohorts, disease-based cohorts, and hospital biobank collections linked to nationwide health registries, has been previously described.[12] A detailed ethics statement is provided in the Data Supplement (online only). In Finland, the population-based breast cancer screening program is managed by local authorities, and all screenings are monitored through the Mass Screening Registry for breast cancer, maintained by the Finnish Cancer Registry (FCR). We used FinnGen Data Freeze 9, studying women free from breast cancer in the beginning of 1992 with ≥1 screening invitation between 1992 and 2019 within the Mass Screening Registry. We identified the breast cancer cases from the FCR (available since 1953; nationwide completeness of breast cancer at 99.5%[13]) with International Classification of Diseases for Oncology (ICD-O-3 C50*), and from the nationwide death registry with ICD-10 C50* (available since 1969).

In Finland, biennial mammographic screening is offered to all women between age 50 and 69 years. Breast cancer cases were classified into the following three categories, following previous classification[11]: (1) *nonattendees*—nonparticipation in the previous screening, (2) *screen-detected*—a positive screening result (malignant histologic finding assigned to follow-up examinations or surgery) and a breast cancer diagnosis within 6 months after screening, and (3) *interval*—negative result in the previous screening or diagnosis later than 6 months from the screening. Our category frequencies are in line with age-matched proportions from nationwide data from the Mass Screening Register (Data Supplement, Table S1). Positive predictive value (PPV) was defined as the proportion of women diagnosed with breast cancer out of women with a positive screening finding, defined as women called back for a complementary follow-up examination (ultrasound with or without biopsy or additional imaging; most being biopsies) or surgery because of an abnormal screening mammogram.

PRS, PVs, and FH

We used a previously published genomewide breast cancer PRS,[10] which has shown similar performance in another study.[14] In short, the PRS was built with the software PRS-CS which applies continuous shrinkage (CS) priors, using summary statistics from a large genomewide association study independent of FinnGen. The PRS consists of 1,079,089 variants (PGS Catalog ID PGS000335). The PRS was studied either as a (1) continuous variable (per standard deviation [SD] increment), (2) by deciles, or (3) divided into three categories, with high PRS defined as the top decile of the PRS distribution (>90th percentile), low PRS as the bottom decile (<10th), with average risk (10th-90th) as reference to contrast the effect sizes to the average population.

The PV carriers were identified from the genotypes, and we studied three variants: *CHEK2* c.1100delC, *CHEK2*

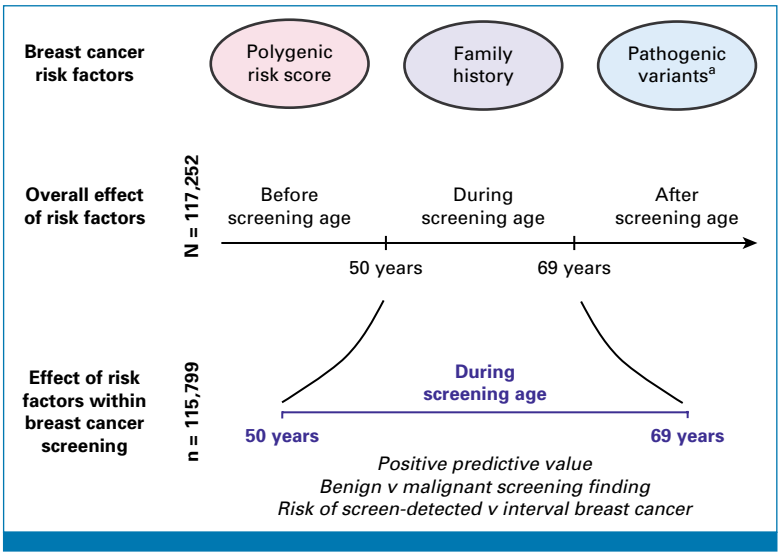

FIG 1. Study overview. [a]Most frequent susceptibility genes in Finland (*CHEK2* and *PALB2*).

c.319+2T>A, and *PALB2* c.1592delT, which are, respectively, 3.7-, 19.7-, and 242-fold enriched in the Finnish population compared with Non-Finnish-Swedish-Estonian Europeans.[15] The *CHEK2* variants are considered moderate-risk variants in Finland and the *PALB2* a high-risk variant. These represent the most frequent breast cancer susceptibility genes within Finland, and the variants are identified with high quality on the genotyping array used in FinnGen. Variants were analyzed jointly to increase power. We used a registry-based composite end point for FH, identified through (1) parental causes of death from the death registry, (2) study participants' ICD-10 diagnoses denoting FH, and (3) by identifying breast cancers of the study participants' first-degree relatives included in FinnGen. Further information on genotyping, imputation, PRS, PVs, and FH is provided in the Data Supplement.

Statistical Analysis

For the general performance of PRS across the data, the start of the follow-up was set to birth, with follow-up ending at diagnosis of invasive breast cancer on in situ lesions, death, or on December 31, 2019. Hazard ratios (HRs) and their 95% CIs were estimated with Cox proportional hazards model implemented in *survival* package in R. Regression models were adjusted with birth year, genotyping array, subcohort, and the first 10 principal components of genetic ancestry. Statistical analyses (Data Supplement) were performed with R 4.1.2.

RESULTS

The current target age of the national screening program in Finland is biennial screening between age 50 and 69 years. Among all 117,252 women invited for a breast cancer screen, we first studied their overall effects on breast cancer risk before, during, and after screening age, for evaluating the performance of PRS compared with PVs and FH in each age group (Fig 1). We then evaluated the impact of the risk factors on screening events and metrics. Among the 117,252 women, we observed 11,556 breast cancer cases, of which 10,570 (91.6%) were invasive and 974 (8.4%) were in situ breast cancers (12 with missing information). One thousand four hundred fifty-three with prevalent breast cancer before the screening start were excluded from analyses on women of screening age.

The three variants were analyzed jointly (2,437 mutation carriers, 2.1%; *CHEK2* c.1100delC 1.6%, *CHEK2* c.319+2T>A 0.2%, and *PALB2* c.1592delT 0.3%). FH of breast cancer was defined through health care registries on the basis of parental causes of death, first-degree relatives in FinnGen diagnosed with breast cancer, or an ICD-10 diagnosis for FH (Methods).

Stratifying the three risk factors into three age groups (Table 1), the HRs of PRS, PVs, and FH decreased with increasing age, and the highest effect sizes were observed in the group before screening age. Similar patterns and effect sizes were observed for all three risk factors, with high PRS (>90th percentile of the PRS distribution) being the most common risk factor. Effect sizes by PRS decile are provided in the Data Supplement (Table S2).

Figure 2 and the Data Supplement (Fig S1) show lifetime risks of breast cancer for the risk factors and their combinations, and indicate when each group reaches a 2% cumulative incidence, aligning with the population's average at the start of organized screening at age 50 years. This age provides a guideline for when to begin screening on the basis of

TABLE 1. Study Characteristics and Associations Between Breast Cancer and PRS, PVs, and FH

Category	Before Screening Age	During Screening Age	After Screening Age
Any breast cancer, No.	1,453	7,905	2,198
Invasive breast cancer, No.	1,377	7,145	2,058
In situ breast cancer, No.	74	760	140
Bilateral breast cancer, No.	20	96	36
Age at disease onset, years, median (IQR)	45.9 (42.9-47.9)	59.1 (54.2-64.1)	73.5 (70.1-76.7)
PRS >90% in cases, No. (%)	341 (23.5)	1,663 (21.0)	404 (18.4)
PRS >90% in controls, No. (%)	11,210 (9.9)	9,547 (8.8)	3,652 (8.5)
PV carriers in cases, No. (%)	94 (6.5)	345 (4.4)	73 (3.3)
PV carriers in controls, No. (%)	2,343 (2.0)	1,998 (1.9)	740 (1.7)
Positive FH in cases, No. (%)	107 (7.4)	489 (6.2)	53 (2.4)
Positive FH in controls, No. (%)	3,605 (31)	3,116 (2.9)	865 (2.0)
HR (95% CI) for PRS, continuous			
Any breast cancer	1.78 (1.69 to 1.87)	1.66 (1.63 to 1.70)	1.63 (1.56 to 1.70)
Invasive breast cancer	1.75 (1.66 to 1.84)	1.67 (1.63 to 1.71)	1.64 (1.57 to 1.71)
In situ breast cancer	2.39 (1.91 to 3.00)	1.73 (1.61 to 1.86)	1.58 (1.33 to 1.87)
Bilateral breast cancer	—	2.49 (2.03 to 3.05)	2.75 (1.96 to 3.85)
HR (95% CI) for PRS, PRS >90% *v* 10%-90%			
Any breast cancer	2.50 (2.21 to 2.83)	2.38 (2.25 to 2.51)	2.11 (1.90 to 2.36)
Invasive breast cancer	2.45 (2.16 to 2.79)	2.40 (2.26 to 2.54)	2.07 (1.85 to 2.31)
In situ breast cancer	3.62 (2.20 to 5.94)	2.51 (2.10 to 2.99)	3.14 (2.10 to 4.68)
Bilateral breast cancer	—	4.71 (3.07 to 7.23)	—
HR (95% CI) for PVs			
Any breast cancer	3.13 (2.53 to 3.86)	2.30 (2.06 to 2.56)	1.95 (1.54 to 2.47)
Invasive breast cancer	3.12 (2.51 to 3.87)	2.31 (2.06 to 2.59)	1.93 (1.51 to 2.47)
In situ breast cancer	—	2.43 (1.71 to 3.45)	—
Bilateral breast cancer	—	4.37 (2.01 to 9.51)	—
HR (95% CI) for FH			
Any breast cancer	1.97 (1.62 to 2.40)	1.96 (1.79 to 2.15)	1.68 (1.28 to 2.21)
Invasive breast cancer	2.00 (1.64 to 2.46)	2.02 (1.83 to 2.22)	1.72 (1.30 to 2.27)
In situ breast cancer	—	1.62 (1.17 to 2.25)	—
Bilateral breast cancer	—	5.04 (2.74 to 9.29)	—

NOTE. Cells containing — were not assessed because of small case counts. PVs: *CHEK2* c.1100delC, *CHEK2* c.319+2T>A, *PALB2* c.1592delT, analyzed jointly for power, and heterozygotes were considered jointly with homozygotes. Of the 152 bilateral breast cancers, 144 were invasive breast cancers and eight were in situ cancers (on the basis of the most severe lesion). Twelve individuals had missing data on information about in situ versus invasive breast cancer. For before screening age (age <49 years), women diagnosed during or after screening age were considered as controls. For during screening age, women diagnosed after screening age were considered as controls, and cases diagnosed before screening age were excluded. For after screening age (age >71 years), women diagnosed before or during screening age were excluded. Analyses for in situ breast cancer excluded invasive breast cancer cases and vice versa. Similarly, analyses on bilateral breast cancer excluded nonbilateral breast cancer cases.

Abbreviations: FH, family history; HR, hazard ratio; PRS, polygenic risk score; PV, pathogenic variant.

individual risk. Groups of high PRS, PV carriers, or positive FH reached this 2% prevalence at age 42 years, while women with high PRS and FH or PV reached it at age 38 years. By contrast, women without PVs or FH who have a low PRS reached a similar risk level two decades later, at age 62 years. The estimates are calibrated to the general population (see the Data Supplement for details).

The screening events and metrics were studied in 115,799 individuals (excluding 1,453 women with breast cancer before first screening invitation). Of the 7,905 breast cancers diagnosed during the screening age window, 4,691 (59.3% of all) were screen-detected breast cancers (of which 11.8% in situs), 1,880 (23.8% of all) were interval breast cancers (7.0% in situs), and 1,334 (16.9% of all) were nonattendee breast cancers (nonparticipation in previous screening, 5.6% in situs). The overall screening participation rate for the 693,730 screening invitations was 88.5%. One hundred thirteen thousand nine hundred sixty-nine (97.0%) women had participated at least once in

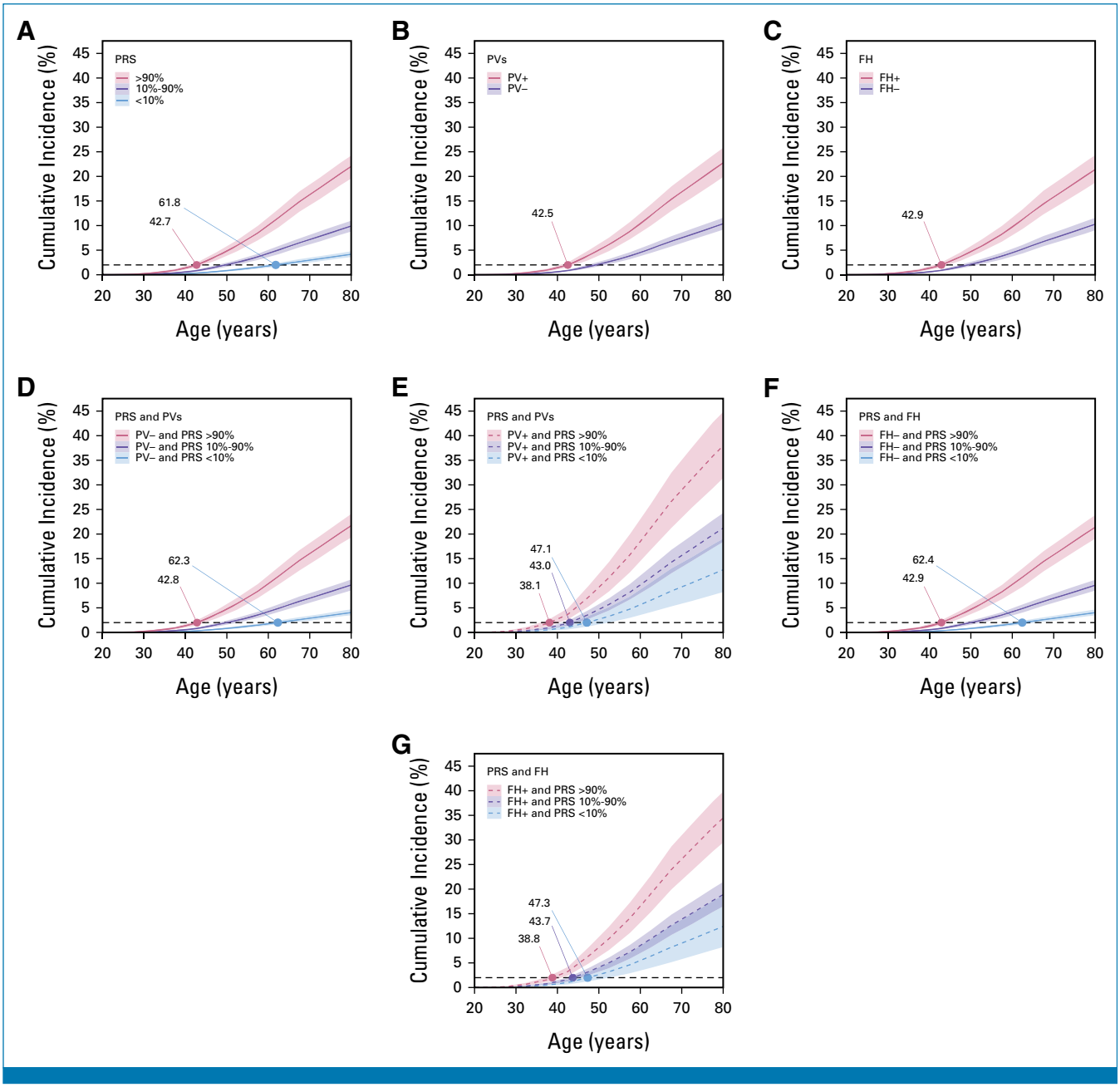

FIG 2. Lifetime risk of breast cancer for categories of (A) PRS, by carrier status for (B) PV, (C) FH status, (D and E) the combination of PRS and PVs, and (F and G) the combination of PRS and FH. The numbers indicate when each category reaches a 2% cumulative incidence, aligning with the population's average at the start of organized screening at age 50 years. The cumulative incidences by PRS decile are provided in the Data Supplement (Fig S1). The estimates are calibrated to the general population, with the estimates accounting for competing risks of death from other causes than breast cancer (see the Data Supplement for details). FH, family history; PRS, polygenic risk score; PV, pathogenic variant.

a screening (mean 5.4 screenings, SD 2.8, mean age at individual screenings 57.3 years, SD 4.9).

PPV

For each of the three risk factors, we assessed the PPV (proportion of women diagnosed with breast cancer out of women with a positive screening finding, defined as women called back for a complementary follow-up examination for an abnormal screening mammogram; see Methods for details). Of all screening events, 3.1% of women were referred for follow-up examinations, of whom 25.0% were diagnosed with breast cancer (0.8% of all screenings).

The PPVs increased considerably as a function of the PRS (Fig 3A), ranging from 12.7% (95% CI, 11.0 to 14.6) in the lowest PRS decile to 39.5% (95% CI, 37.6 to 41.5) in the highest decile. Similarly, being a PV carrier or having positive

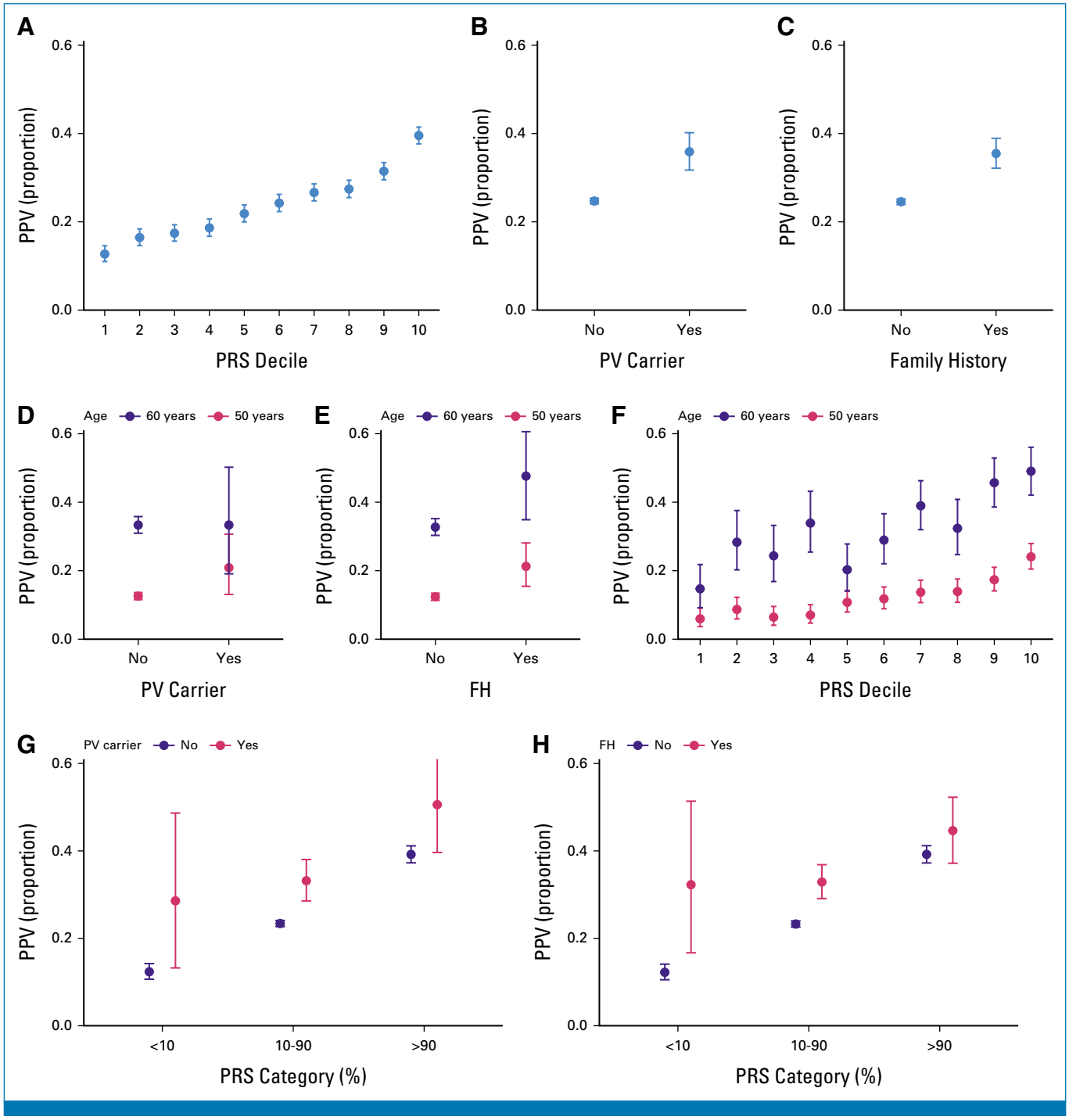

FIG 3. Observed PPV (proportion of screen-detected cancers among women with a screening finding defined as women called back for complementary follow-up examination for an abnormal screening mammogram; see Methods for details) with different risk factors. The PPV (A) by PRS decile, (B) by PV carrier status, and (C) by FH status, with corresponding PPVs for two screening ages, (D-F) 50 and 60 years. (D-F) Also highlight the impact of age on PPV, because of differences in baseline risk of breast cancer, which increases with age. (G and H) The PPV by combinations of (G) PRS and PV carrier and (H) PRS and FH status, with PRS divided into three categories. PPVs at all screening ages (biennially from age 50 years to 69 years) are provided in the Data Supplement (Fig S2), and the detailed numbers for the Figure are provided in the Data Supplement (Table S1). Error bars show the 95% CIs. PVs: *CHEK2* c.1100delC, *CHEK2* c.319+2T>A, *PALB2* c.1592delT, analyzed jointly for power, and heterozygotes were considered jointly with homozygotes. FH, family history; PPV, positive predictive value; PRS, polygenic risk score; PV, pathogenic variant.

FH both increased the PPV (Figs 3B and 3C), with the PPVs slightly lower than what we observed for the highest PRS decile (35.9% [95% CI, 31.7 to 40.2%] for PV carriers; 35.5% [95% CI, 32.1 to 38.9] for positive FH). Combinations of PRS

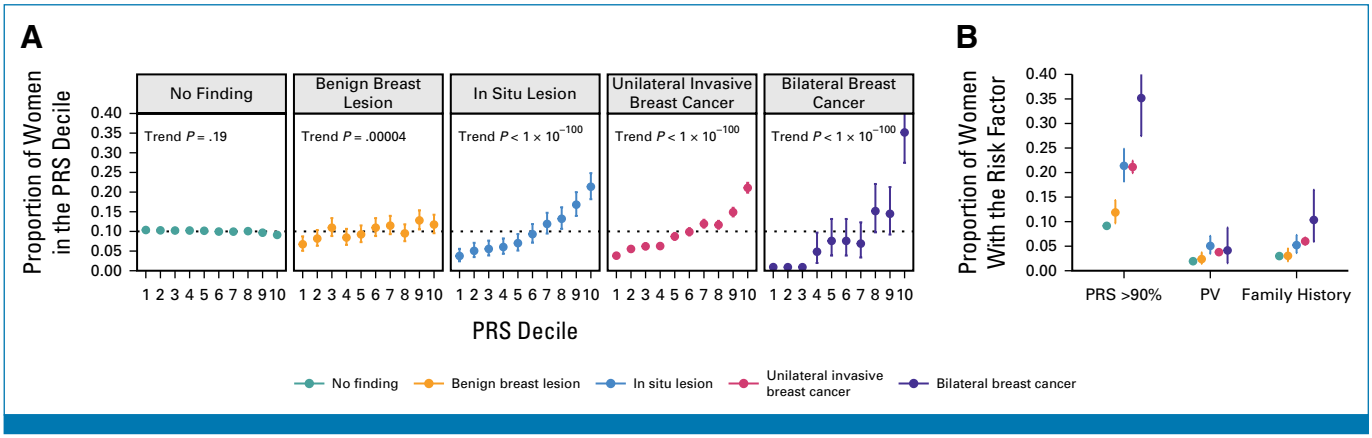

FIG 4. Proportion of individuals with risk factors by type of most severe screening finding. Women with no finding have never had a positive screening finding. (A) Prevalence of women in different PRS deciles by screening finding. Each PRS decile contains by definition 10% of individuals (dotted line), whereby proportions over 10% indicate enrichment of the histologic finding. For instance, of women with bilateral breast cancer, 35.2% (95% CI, 27.4 to 43.5) had a PRS in the top decile. (B) Prevalence of each risk factor (PRS category, PV carrier, and family history) in women by screening finding. The PRS >90% contains the same information as the top deciles for each screening finding in (A). In addition to the final breast cancer diagnosis available in the Finnish Cancer Registry, information on histology from screening biopsies is available within the Mass Screening Registry, on the basis of ICD-O-3 morphology codes. The screening findings were divided into the following categories, with each woman classified on the basis of her most severe screening finding: (1) no finding (ie, no suspicion of malignancy, N = 110,185), (2) benign (nonmalignant) breast lesion (N = 758), (3) in situ lesion (N = 613), (4) unilateral invasive breast cancer (N = 4,098), and (5) bilateral breast cancer (N = 145; in situ or invasive lesions simultaneously in both breasts). Because of a small case count, the prevalence of PRS deciles one to three for bilateral breast cancer was calculated by pooling their prevalence and dividing it by three. Error bars show the 95% CIs. The *P* value for trend was calculated by randomly sampling 1,000 individuals in screening finding categories that had over 1,000 individuals (the categories were no finding and unilateral invasive breast cancer). PVs: *CHEK2* c.1100delC, *CHEK2* c.319+2T>A, *PALB2* c.1592delT, analyzed jointly for power, and heterozygotes were considered jointly with homozygotes. ICD-O, International Classification of Diseases for Oncology; PRS, polygenic risk score; PV, pathogenic variant.

with PVs or FH risk led to the highest PPVs (Figs 3G and 3H). Women with positive FH and high PRS (>90%) had a PPV of 44.6% (95% CI, 37.2 to 52.3) and PV carriers with high PRS had an even higher PPV at 50.6% (95% CI, 39.6 to 61.5). In individuals with low PRS, FH and PVs had a particularly strong impact, although with wide CIs. As baseline risk increases with age, we also assessed the risk factors by screening age and observed clear PPV trends by age (Fig 3D-3F). Detailed PPVs, and PPVs by PRS decile for all ages are provided in the Data Supplement (Table S3 and Fig S2, respectively).

Mammography Screening Findings

We first assessed the proportion of cases in each category by PRS decile (Fig 4A). By definition, each PRS decile contains 10% of individuals, whereby proportions over 10% indicate enrichment of a screening finding. The proportion of cases was evenly distributed across PRS deciles for no findings and for benign breast lesions, whereas both in situ lesions and invasive breast cancers were in a similar manner enriched for high PRS. The highest enrichment was observed for high PRS for bilateral breast cancer, where 35.2% (95% CI, 27.4 to 43.5) of the cases had a high PRS (>90th percentile).

Next, we assessed the prevalence of high PRS, PVs, and FH by the most severe screening finding (Fig 4B). Being a PV carrier or having positive FH was less common than a high PRS, and similar to PRS, the risk factors were not enriched in women with benign breast lesions, and they did not distinguish women with situ lesions and invasive breast cancer. Similar to PRS, positive FH was enriched in women with bilateral breast cancer, with 10.3% (95% CI, 5.9 to 16.5) of the cases having positive FH.

Impact of Polygenic Risk on Screen- and Interval-Detected Breast Cancers

In women with high PRS, the effect size for screen-detected and interval breast cancers was similar: at the screening at age 50 years, the HR was 3.09 (95% CI, 2.38 to 4.03) for screen-detected and HR 2.78 (95% CI, 2.00 to 3.86) for interval breast cancer, with no clear trends for effect size by age or systematic differential effects by detection type (Data Supplement, Table S4). Women with a high PRS with a negative screen had an elevated risk for interval breast cancer, and a screen-detected cancer in the next screen (Fig 5, Data Supplement, Fig S3). Cumulative incidences for interval breast cancer by 1 year and 2 years after the negative screen, and for screen-detected breast cancer are provided in the Data Supplement (Table S5). For instance, at age 50 years, the cumulative incidence of interval breast cancer for PRS >90% was at 1 year 0.3% (95% CI, 0.2 to 0.5) and at 2 years 0.7% (95% CI, 0.5 to 0.9). For PRS 10%-90%, the corresponding cumulative incidences are much lower, at 1 year 0.1% (95% CI, 0.1 to 0.1) and at 2 years 0.2% (95% CI, 0.2 to 0.3).

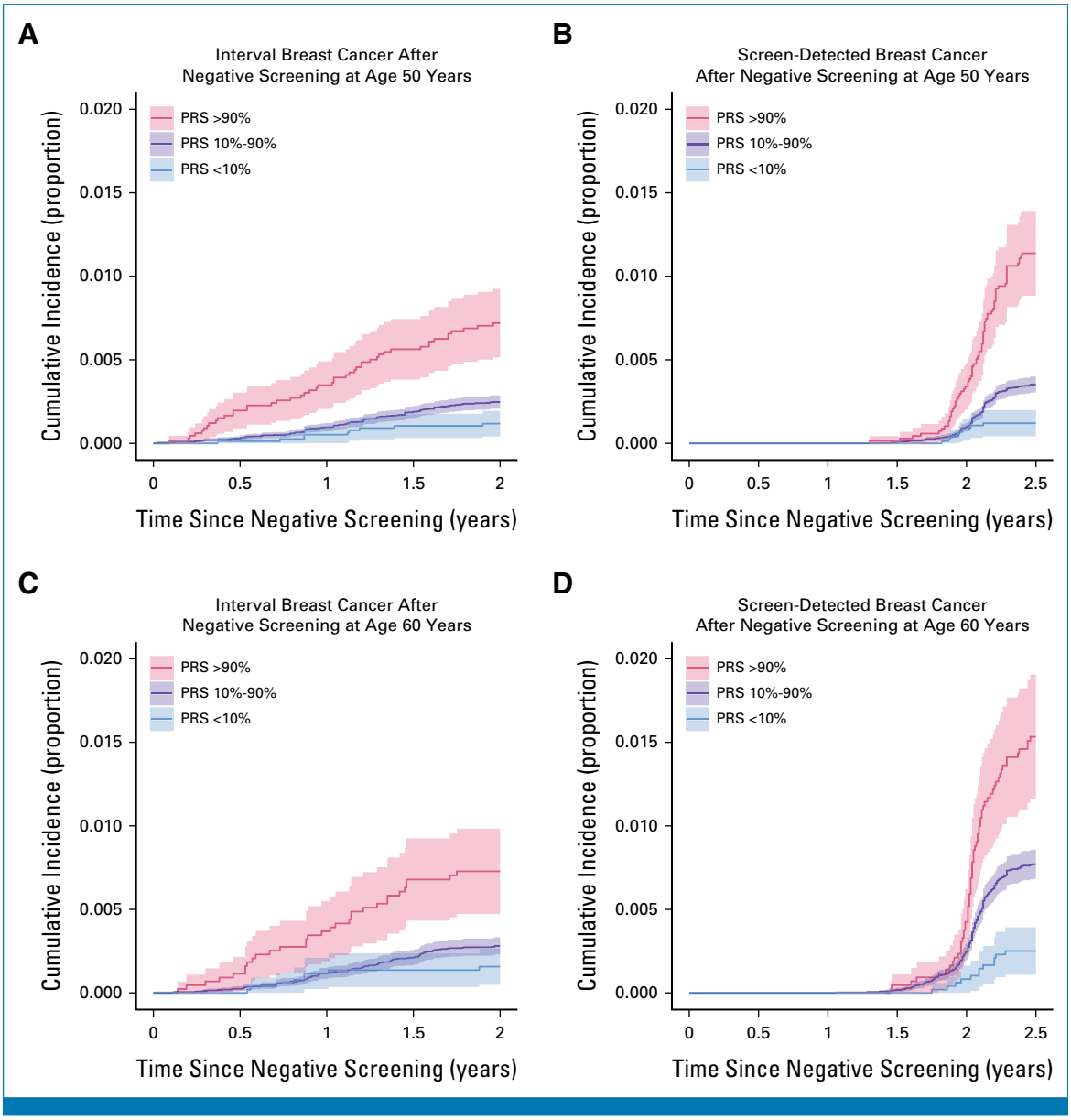

FIG 5. Survival curves showing cumulative incidence of breast cancer for interval and screen-detected cancers after a negative screen at age (A and B) 50 years and (C and D) 60 years by PRS category. Survival curves for a broader set of screening ages are shown in the Data Supplement (Fig S3). Cumulative incidence represents the proportion of individuals diagnosed by each time point shown on the x-axis. PRS, polygenic risk score.

For interval breast cancer, the risk sharply increased with high PRS 2 months after the negative screen at age 50 years. The cumulative incidence of interval breast cancer was low for women with average or low PRS. We did not observe distinct age-related patterns for risk of interval cancer. After a negative screen, the PRS also stratified women according to risk of screen-detected breast cancer in the next screen at all ages, with the cumulative incidence increasing consistently with age, because of baseline risk increases (Data Supplement, Fig S3).

DISCUSSION

PRS studies have recently provided us a broader understanding about the genetic risk factors underlying breast cancer and how it stratifies women on the basis of their future risk of breast cancer, thereby bringing opportunities for risk-tailored screening. We showed the impact of breast cancer PRS on detection of breast cancers in real-life screening data on a large number of women of screening age, comparing the performance of the PRS with PVs and FH, both of which can currently be used for tailoring screening on the basis of individual risk, but which are also not used on a population level. The findings for women with high PRS were similar to PV carriers and women with positive FH, and the risk factors showed complementary performance. The PRS showed clear patterns for a high PRS identifying women more likely to be diagnosed with breast cancer after a positive screening finding, without increasing the detection

rate of benign breast lesions. Women with a high PRS with a negative screening finding had an elevated risk of interval breast cancer, and a screen-detected cancer in the next screen, indicating that women with high PRS could benefit from more frequent screenings. Evaluations of the impact of PRS before screening age also indicated that women with a high PRS could benefit from earlier screening initiation, which in many countries, including Finland, is at age 50 years. On the contrary, women with a low PRS had a very low risk of both interval- and screen-detected cancers, suggesting opportunities for less frequent screens for this low-risk group. The ages at which each risk group reaches a 2% cumulative incidence, aligning with the population at the start of organized screening, provides a guideline for when to begin screening on the basis of individual risk. Cumulative incidences of interval cancer at 1 and 2 years after a negative screen can be used to evaluate the potential impact of incorporating PRS into an annual screening program, depending on the accepted risk levels.

The potential role of breast cancer PRS for stratified screening has previously been evaluated through prospective and retrospective observational studies,[8,16-19] with supporting evidence from cost-effectiveness modeling.[20,21] However, none of these studies have used real-life screening data for screen-detected and interval breast cancers, which is necessary for understanding the impact of PRS in a screening context. Only a few small studies have used such screening data, with most of the studies evaluating PRSs that contain much fewer genetic variants than our genome-wide PRS.[22,23] We linked polygenic risk information to observational population-based data on 693,730 screening events in a country with nationwide biennial mammography screening between age 50 and 69 years and high attendance to the screenings. In addition to a lack of large real-life breast cancer screening studies on breast cancer PRSs, population-scale studies are sparse also for the impact of PVs and FH, but ongoing clinical trials are underway evaluating the performance of personalized breast cancer screening.[24,25]

Risk-tailored surveillance is currently implemented in many countries for women with strong FH of early-onset breast cancer and in many women who have been identified to be carriers of PVs in breast cancer susceptibility genes such as *BRCA1*, *PALB2*, and *CHEK2*. Our results support adding PRS assessment to guide these decisions, as PRS complemented PV and FH information, which we and others have also shown previously.[7,10] In particular, we show that women in the top 10% of the PRS have an elevated risk for interval cancers, showing that these women may benefit for shorter time intervals between screening visits. These women also had an elevated risk for bilateral breast cancer. Moreover, to evaluate the impact of PRSs, PVs, and FH outside of the screening program, we extended the general effect size evaluations to timelines before and after the screening age. We observed similar patterns for all the three risk factors with respect to age, which could support earlier initiation of breast cancer screening in women with high PRS. Second, this study shows that women with low PRS (<10%) had a very low risk of both interval- and screen-detected breast cancers even at age 50 years. At the very least, this argues against benefits of screening women with low PRS and no other risk factors before age 50 years, which is common practice in many countries.[26,27] Further research is needed on the impact of delaying the onset of screening with low PRS.

The large FinnGen study links genotypes to nationwide registries containing 27 years of data on breast cancer screenings and up to 66 years of follow-up within the FCR. The screening attendance and other screening parameters are in line with nationwide data (Data Supplement, Table S1)[11] and the parameters are comparable with reports from other European countries.[27] However, our results are generalizable primarily to countries with biennial screening recommendations. The PVs evaluated are enriched in the Finnish population, allowing reliable identification of carriers. We used a contemporary genomewide PRS outperforming previously published PRSs with a small number of variants.[14]

Despite our substantial sample size, we lacked power to systematically assess risk factor combinations throughout the study or less common *BRCA1* and *BRCA2* PVs, which are rarer in Finland compared with many European countries. The dynamics of PRS and PVs are, however, similar across different susceptibility genes.[9,28] Moreover, the high risk associated with *BRCA1/2* mutations would often necessitate specialized screening protocols beyond traditional organized breast cancer screening.[5] First-degree FH was identified through health care registries, with an effect size comparable with published estimates,[29] and the dynamic between FH and PRS is similar regardless of the source of FH information.[7,8,30,31] Within this registry-based study, variant carriers were not informed of being carriers. The study contains only individuals of European ancestry, but risk- and cost-effectiveness evaluations for breast cancer screening in Asian populations have reached similar conclusions for potential utility for PRSs.[20,32]

Using a large biobank study of women with data from real-life screening events, we show that a breast cancer PRS predicted the outcome of an initial positive screening finding. Moreover, a high PRS was associated with the risk of interval cancer among women with a negative screening result, and with an elevated risk for bilateral breast cancer. The findings support the use of a breast cancer PRS for risk stratification, with optimal stratification reached through combining PRS information with FH of breast cancer and PVs in breast cancer susceptibility genes. Further studies are needed to assess how to optimally integrate these factors into clinical care[33] in addition to assessments of their impact incorporated into a prospective risk-stratified screening program, with cost-effectiveness evaluations.

AFFILIATIONS

[1]Institute for Molecular Medicine Finland, FIMM, HiLIFE, University of Helsinki, Helsinki, Finland
[2]Broad Institute of MIT and Harvard, Cambridge, MA
[3]Helsinki Institute for Information Technology HIIT and Department of Mathematics and Statistics, University of Helsinki, Helsinki, Finland
[4]Department of Public Health, University of Helsinki, Helsinki, Finland
[5]Department of Clinical Genetics, HUSLAB, HUS Diagnostic Center, University of Helsinki and Helsinki University Hospital, Helsinki, Finland
[6]Department of Medical Genetics, University of Helsinki, Helsinki, Finland
[7]Breast Surgery Unit, Comprehensive Cancer Center, Helsinki University Hospital, Helsinki, Finland
[8]University of Helsinki, Helsinki, Finland
[9]Finnish Cancer Registry, Cancer Society of Finland, Helsinki, Finland

CORRESPONDING AUTHOR

Samuli Ripatti, PhD, Institute for Molecular Medicine Finland, FIMM, HiLIFE, University of Helsinki, Helsinki, Finland Faculty of Medicine, University of Helsinki, PO Box 20, FI-00014 University of Helsinki, Finland; Twitter: @samrip; e-mail: samuli.ripatti@helsinki.fi.

PRIOR PRESENTATION

Presented in part at the American Society of Human Genetics Annual Meeting, Los Angeles, CA, October 25-29, 2022.

SUPPORT

Supported by Academy of Finland (grant numbers 331671 and 355567 to N.M., 285380 to S.R., 338507 to M.P.); University of Helsinki HiLIFE Fellows Grant 2023-2025 to N.M.; Finska Läkaresällskapet (to N.M.); Academy of Finland Center of Excellence in Complex Disease Genetics (grant number 312062 to S.R., 336825 to M.P.); European Union's Horizon 2020 research and innovation program under grant agreement No 101016775; the Sigrid Jusélius Foundation (to S.R.); The Finnish Innovation Fund Tekes (grant number 2273/31/2017 to E.W.); Cancer Foundation Finland (to T.M.); and The Doctoral Programme in Population Health, University of Helsinki (to M.T.).

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at DOI https://doi.org/10.1200/JCO.23.00295.

DATA SHARING STATEMENT

The FinnGen data may be accessed through Finnish Biobanks' FinBB portal (www.finbb.fi; email: info.fingenious@finbb.fi). The weights for our polygenic risk scores are available at PGS Catalog (https://www.pgscatalog.org/), PGS ID PGS000335.

AUTHOR CONTRIBUTIONS

Conception and design: Nina Mars, Sini Kerminen, Samuli Ripatti
Collection and assembly of data: Nina Mars, Sirpa Heinävaara, Samuli Ripatti
Data analysis and interpretation: Nina Mars, Sini Kerminen, Kirsimari Aaltonen, Max Tamlander, Matti Pirinen, Eveliina Jakkula, Tuomo Meretoja, Elisabeth Widén, Samuli Ripatti
Manuscript writing: All authors
Final approval of manuscript: All authors
Accountable for all aspects of the work: All authors

ACKNOWLEDGMENT

The authors thank Sari Kivikko, Huei-Yi Shen, and Ulla Tuomainen for management assistance, and Bradley Jermy for methodologic support. The authors want to acknowledge the participants and investigators of FinnGen study. 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 Inc, AstraZeneca UK Ltd, Biogen MA Inc, Bristol Myers Squibb (and Celgene Corporation & Celgene International II Sàrl), Genentech Inc, Merck Sharp & Dohme LCC, Pfizer Inc, GlaxoSmithKline Intellectual Property Development Ltd, Sanofi US Services Inc, Maze Therapeutics Inc, Janssen Biotech Inc, Novartis AG, and Boehringer Ingelheim International GmbH. The following biobanks are acknowledged for delivering biobank samples to FinnGen: Auria Biobank (www.auria.fi/biopankki), THL Biobank (www.thl.fi/biobank), Helsinki Biobank (www.helsinginbiopankki.fi), Biobank Borealis of Northern Finland (https://www.ppshp.fi/Tutkimus-ja-opetus/Biopankki/Pages/Biobank-Borealis-briefly-in-English.aspx), Finnish Clinical Biobank Tampere (www.tays.fi/en-US/Research_and_development/Finnish_Clinical_Biobank_Tampere), Biobank of Eastern Finland (www.ita-suomenbiopankki.fi/en), Central Finland Biobank (www.ksshp.fi/fi-FI/Potilaalle/Biopankki), Finnish Red Cross Blood Service Biobank (www.veripalvelu.fi/verenluovutus/biopankkitoiminta), and Terveystalo Biobank (www.terveystalo.com/fi/Yritystietoa/Terveystalo-Biopankki/Biopankki/). All Finnish Biobanks are members of BBMRI.fi infrastructure (www.bbmri.fi). Finnish Biobank Cooperative-FINBB (https://finbb.fi/) is the coordinator of BBMRI-ERIC operations in Finland.
A list of FinnGen contributors is listed in Appendix Table A1 (online only).

REFERENCES

1. Iwamoto Y, Kaucher S, Lorenz E, et al: Development of breast cancer mortality considering the implementation of mammography screening programs—A comparison of western European countries. BMC Public Health 19:823, 2019
2. Zielonke N, Gini A, Jansen EEL, et al: Evidence for reducing cancer-specific mortality due to screening for breast cancer in Europe: A systematic review. Eur J Cancer 127:191-206, 2020
3. Clift AK, Dodwell D, Lord S, et al: The current status of risk-stratified breast screening. Br J Cancer 126:533-550, 2022
4. Daly MB, Pal T, Berry MP, et al: Genetic/familial high-risk assessment: Breast, ovarian, and pancreatic, version 2.2021, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw 19:77–102, 2021
5. Sessa C, Balmana J, Bober SL, et al: Risk reduction and screening of cancer in hereditary breast-ovarian cancer syndromes: ESMO clinical practice guideline. Ann Oncol 34:33-47, 2023
6. Chatterjee N, Shi J, Garcia-Closas M: Developing and evaluating polygenic risk prediction models for stratified disease prevention. Nat Rev Genet 17:392-406, 2016
7. Mavaddat N, Michailidou K, Dennis J, et al: Polygenic risk scores for prediction of breast cancer and breast cancer subtypes. Am J Hum Genet 104:21-34, 2019
8. Mars N, Koskela JT, Ripatti P, et al: Polygenic and clinical risk scores and their impact on age at onset and prediction of cardiometabolic diseases and common cancers. Nat Med 26:549-557, 2020
9. Fahed AC, Wang M, Homburger JR, et al: Polygenic background modifies penetrance of monogenic variants for tier 1 genomic conditions. Nat Commun 11:3635, 2020
10. Mars N, Widén E, Kerminen S, et al: The role of polygenic risk and susceptibility genes in breast cancer over the course of life. Nat Commun 11:6383, 2020
11. Sarkeala T, Luostarinen T, Dyba T, et al: Breast carcinoma detection modes and death in a female population in relation to population-based mammography screening. Springerplus 3:348, 2014
12. Kurki MI, Karjalainen J, Palta P, et al: FinnGen provides genetic insights from a well-phenotyped isolated population. Nature 613:508-518, 2023

13. Leinonen MK, Miettinen J, Heikkinen S, et al: Quality measures of the population-based Finnish Cancer Registry indicate sound data quality for solid malignant tumours. Eur J Cancer 77:31-39, 2017
14. Mars N, Kerminen S, Feng Y-CA, et al: Genome-wide risk prediction of common diseases across ancestries in one million people. Cell Genom 2:100118, 2022
15. Karczewski KJ, Francioli LC, Tiao G, et al: The mutational constraint spectrum quantified from variation in 141,456 humans. Nature 581:434-443, 2020
16. Evans DGR, Harkness EF, Brentnall AR, et al: Breast cancer pathology and stage are better predicted by risk stratification models that include mammographic density and common genetic variants. Breast Cancer Res Treat 176:141-148, 2019
17. Lee A, Mavaddat N, Wilcox AN, et al: BOADICEA: A comprehensive breast cancer risk prediction model incorporating genetic and nongenetic risk factors. Genet Med 21:1708-1718, 2019
18. Lall K, Lepamets M, Palover M, et al: Polygenic prediction of breast cancer: Comparison of genetic predictors and implications for risk stratification. BMC Cancer 19:557, 2019
19. van den Broek JJ, Schechter CB, van Ravesteyn NT, et al: Personalizing breast cancer screening based on polygenic risk and family history. J Natl Cancer Inst 113:434-442, 2021
20. Wong JZY, Chai JH, Yeoh YS, et al: Cost effectiveness analysis of a polygenic risk tailored breast cancer screening programme in Singapore. BMC Health Serv Res 21:379, 2021
21. Pashayan N, Morris S, Gilbert FJ, et al: Cost-effectiveness and benefit-to-harm ratio of risk-stratified screening for breast cancer: A life-table model. JAMA Oncol 4:1504-1510, 2018
22. Li J, Holm J, Bergh J, et al: Breast cancer genetic risk profile is differentially associated with interval and screen-detected breast cancers. Ann Oncol 26:517-522, 2015
23. Grassmann F, He W, Eriksson M, et al: Interval breast cancer is associated with other types of tumors. Nat Commun 10:4648, 2019
24. Shieh Y, Eklund M, Madlensky L, et al: Breast cancer screening in the precision medicine era: Risk-based screening in a population-based trial. J Natl Cancer Inst 109:djw290, 2017
25. Roux A, Cholerton R, Sicsic J, et al: Study protocol comparing the ethical, psychological and socio-economic impact of personalised breast cancer screening to that of standard screening in the "My Personal Breast Screening" (MyPeBS) randomised clinical trial. BMC Cancer 22:507, 2022
26. Ren W, Chen M, Qiao Y, et al: Global guidelines for breast cancer screening: A systematic review. Breast 64:85-99, 2022
27. Ponti A, Anttila A, Ronco G, et al: Cancer Screening in the European Union (2017). Report on the implementation of the Council Recommendation on cancer screening (second report). https://screening.iarc.fr/EUreport.php
28. Gallagher S, Hughes E, Wagner S, et al: Association of a polygenic risk score with breast cancer among women carriers of high- and moderate-risk breast cancer genes. JAMA Netw Open 3: e208501, 2020
29. Brewer HR, Jones ME, Schoemaker MJ, et al: Family history and risk of breast cancer: An analysis accounting for family structure. Breast Cancer Res Treat 165:193-200, 2017
30. Mars N, Lindbohm JV, Della Briotta Parolo P, et al: Systematic comparison of family history and polygenic risk across 24 common diseases. Am J Hum Genet 109:2152-2162, 2022
31. Li H, Feng B, Miron A, et al: Breast cancer risk prediction using a polygenic risk score in the familial setting: A prospective study from the Breast Cancer Family Registry and kConFab. Genet Med 19: 30-35, 2017
32. Ho WK, Tan MM, Mavaddat N, et al: European polygenic risk score for prediction of breast cancer shows similar performance in Asian women. Nat Commun 11:3833, 2020
33. Menko FH, Monkhorst K, Hogervorst FBL, et al: Challenges in breast cancer genetic testing. A call for novel forms of multidisciplinary care and long-term evaluation. Crit Rev Oncol Hematol 176: 103642, 2022

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Comprehensive Inherited Risk Estimation for Risk-Based Breast Cancer Screening in Women

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated unless otherwise noted. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/rwc or ascopubs.org/jco/authors/author-center.

Open Payments is a public database containing information reported by companies about payments made to US-licensed physicians (Open Payments).

Sini Kerminen
Employment: Nightingale Health PLC
Stock and Other Ownership Interests: Nightingale Health PLC
Research Funding: Nightingale Health PLC

No other potential conflicts of interest were reported.

APPENDIX

TABLE A1. FinnGen

Full Name	Affiliation
Aarno Palotie	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland; Broad Institute of MIT and Harvard; Massachusetts General Hospital
Mark Daly	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland; Broad Institute of MIT and Harvard; Massachusetts General Hospital
Bridget Riley-Gills	AbbVie, Chicago, IL
Howard Jacob	AbbVie, Chicago, IL
Dirk Paul	Astra Zeneca, Cambridge, United Kingdom
Athena Matakidou	Astra Zeneca, Cambridge, United Kingdom
Adam Platt	Astra Zeneca, Cambridge, United Kingdom
Heiko Runz	Biogen, Cambridge, MA
Sally John	Biogen, Cambridge, MA
George Okafo	Boehringer Ingelheim, Ingelheim am Rhein, Germany
Nathan Lawless	Boehringer Ingelheim, Ingelheim am Rhein, Germany
Robert Plenge	Bristol Myers Squibb, New York, NY
Joseph Maranville	Bristol Myers Squibb, New York, NY
Mark McCarthy	Genentech, San Francisco, CA
Julie Hunkapiller	Genentech, San Francisco, CA
Margaret G. Ehm	GlaxoSmithKline, Collegeville, PA
Kirsi Auro	GlaxoSmithKline, Espoo, Finland
Simonne Longerich	Merck, Kenilworth, NJ
Caroline Fox	Merck, Kenilworth, NJ
Anders Mälarstig	Pfizer, New York, NY
Katherine Klinger	Translational Sciences, Sanofi R&D, Framingham, MA
Deepak Raipal	Translational Sciences, Sanofi R&D, Framingham, MA
Eric Green	Maze Therapeutics, San Francisco, CA
Robert Graham	Maze Therapeutics, San Francisco, CA
Robert Yang	Janssen Biotech, Beerse, Belgium
Chris O'Donnell	Novartis Institutes for BioMedical Research, Cambridge, MA
Tomi P. Mäkelä	HiLIFE, University of Helsinki, Finland, Finland
Jaakko Kaprio	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Petri Virolainen	Auria Biobank/University of Turku/Hospital District of Southwest Finland, Turku, Finland
Antti Hakanen	Auria Biobank/University of Turku/Hospital District of Southwest Finland, Turku, Finland
Terhi Kilpi	THL Biobank/Finnish Institute for Health and Welfare (THL), Helsinki, Finland
Markus Perola	THL Biobank/Finnish Institute for Health and Welfare (THL), Helsinki, Finland
Jukka Partanen	Finnish Red Cross Blood Service/Finnish Hematology Registry and Clinical Biobank, Helsinki, Finland
Anne Pitkäranta	Helsinki Biobank/Helsinki University and Hospital District of Helsinki and Uusimaa, Helsinki
Juhani Junttila	Northern Finland Biobank Borealis/University of Oulu/Northern Ostrobothnia Hospital District, Oulu, Finland
Raisa Serpi	Northern Finland Biobank Borealis/University of Oulu/Northern Ostrobothnia Hospital District, Oulu, Finland
Tarja Laitinen	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
Jari Laukkanen	Central Finland Biobank/University of Jyväskylä/Central Finland Health Care District, Jyväskylä, Finland
Marco Hautalahti	FINBB—Finnish Biobank Cooperative
Outi Tuovila	Business Finland, Helsinki, Finland
Raimo Pakkanen	Business Finland, Helsinki, Finland
Jeffrey Waring	AbbVie, Chicago, IL
Bridget Riley-Gillis	AbbVie, Chicago, IL

(continued on following page)

TABLE A1. FinnGen (continued)

Full Name	Affiliation
Fedik Rahimov	AbbVie, Chicago, IL
Ioanna Tachmazidou	Astra Zeneca, Cambridge, United Kingdom
Chia-Yen Chen	Biogen, Cambridge, MA
Heiko Runz	Biogen, Cambridge, MA
Zhihao Ding	Boehringer Ingelheim, Ingelheim am Rhein, Germany
Marc Jung	Boehringer Ingelheim, Ingelheim am Rhein, Germany
Shameek Biswas	Bristol Myers Squibb, New York, NY
Rion Pendergrass	Genentech, San Francisco, CA
Julie Hunkapiller	Genentech, San Francisco, CA
Margaret G. Ehm	GlaxoSmithKline, Collegeville, PA
David Pulford	GlaxoSmithKline, Stevenage, United Kingdom
Neha Raghavan	Merck, Kenilworth, NJ
Adriana Huertas-Vazquez	Merck, Kenilworth, NJ
Jae-Hoon Sul	Merck, Kenilworth, NJ
Anders Mälarstig	Pfizer, New York, NY
Xinli Hu	Pfizer, New York, NY
Katherine Klinger	Translational Sciences, Sanofi R&D, Framingham, MA
Robert Graham	Maze Therapeutics, San Francisco, CA
Eric Green	Maze Therapeutics, San Francisco, CA
Sahar Mozaffari	Maze Therapeutics, San Francisco, CA
Dawn Waterworth	Janssen Research & Development, LLC, Spring House, PA
Nicole Renaud	Novartis Institutes for BioMedical Research, Cambridge, MA
Ma'en Obeidat	Novartis Institutes for BioMedical Research, Cambridge, MA
Samuli Ripatti	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Johanna Schleutker	Auria Biobank/University of Turku/Hospital District of Southwest Finland, Turku, Finland
Markus Perola	THL Biobank/Finnish Institute for Health and Welfare (THL), Helsinki, Finland
Mikko Arvas	Finnish Red Cross Blood Service/Finnish Hematology Registry and Clinical Biobank, Helsinki, Finland
Olli Carpén	Helsinki Biobank/Helsinki University and Hospital District of Helsinki and Uusimaa, Helsinki
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
Arto Mannermaa	Biobank of Eastern Finland/University of Eastern Finland/Northern Savo Hospital District, Kuopio, Finland
Katriina Aalto-Setälä	Faculty of Medicine and Health Technology, Tampere University, Tampere, Finland
Mika Kähönen	Finnish Clinical Biobank Tampere/University of Tampere/Pirkanmaa Hospital District, Tampere, Finland
Jari Laukkanen	Central Finland Biobank/University of Jyväskylä/Central Finland Health Care District, Jyväskylä, Finland
Johanna Mäkelä	FINBB—Finnish Biobank Cooperative
Reetta Kälviäinen	Northern Savo Hospital District, Kuopio, Finland
Valtteri Julkunen	Northern Savo Hospital District, Kuopio, Finland
Hilkka Soininen	Northern Savo Hospital District, Kuopio, Finland
Anne Remes	Northern Ostrobothnia Hospital District, Oulu, Finland
Mikko Hiltunen	University of Eastern Finland, Kuopio, Finland
Jukka Peltola	Pirkanmaa Hospital District, Tampere, Finland
Minna Raivio	Hospital District of Helsinki and Uusimaa, Helsinki, Finland
Pentti Tienari	Hospital District of Helsinki and Uusimaa, Helsinki, Finland
Juha Rinne	Hospital District of Southwest Finland, Turku, Finland
Roosa Kallionpää	Hospital District of Southwest Finland, Turku, Finland
Juulia Partanen	Institute for Molecular Medicine Finland, HiLIFE, University of Helsinki, Finland
Ali Abbasi	AbbVie, Chicago, IL
Adam Ziemann	AbbVie, Chicago, IL
Nizar Smaoui	AbbVie, Chicago, IL

(continued on following page)

TABLE A1. FinnGen (continued)

Full Name	Affiliation
Anne Lehtonen	AbbVie, Chicago, IL
Susan Eaton	Biogen, Cambridge, MA
Heiko Runz	Biogen, Cambridge, MA
Sanni Lahdenperä	Biogen, Cambridge, MA
Shameek Biswas	Bristol Myers Squibb, New York, NY
Julie Hunkapiller	Genentech, San Francisco, CA
Natalie Bowers	Genentech, San Francisco, CA
Edmond Teng	Genentech, San Francisco, CA
Rion Pendergrass	Genentech, San Francisco, CA
Fanli Xu	GlaxoSmithKline, Brentford, United Kingdom
David Pulford	GlaxoSmithKline, Stevenage, United Kingdom
Kirsi Auro	GlaxoSmithKline, Espoo, Finland
Laura Addis	GlaxoSmithKline, Brentford, United Kingdom
John Eicher	GlaxoSmithKline, Brentford, United Kingdom
Qingqin S Li	Janssen Research & Development, LLC, Titusville, NJ 08560
Karen He	Janssen Research & Development, LLC, Spring House, PA
Ekaterina Khramtsova	Janssen Research & Development, LLC, Spring House, PA
Neha Raghavan	Merck, Kenilworth, NJ
Martti Färkkilä	Hospital District of Helsinki and Uusimaa, Helsinki, Finland
Jukka Koskela	Hospital District of Helsinki and Uusimaa, Helsinki, Finland
Sampsa Pikkarainen	Hospital District of Helsinki and Uusimaa, Helsinki, Finland
Airi Jussila	Pirkanmaa Hospital District, Tampere, Finland
Katri Kaukinen	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
Mark Daly	Institute for Molecular Medicine, Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland; Broad Institute of MIT and Harvard; Massachusetts General Hospital
Ali Abbasi	AbbVie, Chicago, IL
Jeffrey Waring	AbbVie, Chicago, IL
Nizar Smaoui	AbbVie, Chicago, IL
Fedik Rahimov	AbbVie, Chicago, IL
Anne Lehtonen	AbbVie, Chicago, IL
Tim Lu	Genentech, San Francisco, CA
Natalie Bowers	Genentech, San Francisco, CA
Rion Pendergrass	Genentech, San Francisco, CA
Linda McCarthy	GlaxoSmithKline, Brentford, United Kingdom
Amy Hart	Janssen Research & Development, LLC, Spring House, PA
Meijian Guan	Janssen Research & Development, LLC, Spring House, PA
Jason Miller	Merck, Kenilworth, NJ
Kirsi Kalpala	Pfizer, New York, NY
Melissa Miller	Pfizer, New York, NY
Xinli Hu	Pfizer, New York, NY
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
Nina Mars	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland

(continued on following page)

TABLE A1. FinnGen (continued)

Full Name	Affiliation
Ali Abbasi	AbbVie, Chicago, IL
Jeffrey Waring	AbbVie, Chicago, IL
Fedik Rahimov	AbbVie, Chicago, IL
Apinya Lertratanakul	AbbVie, Chicago, IL
Nizar Smaoui	AbbVie, Chicago, IL
Anne Lehtonen	AbbVie, Chicago, IL
David Close	Astra Zeneca, Cambridge, United Kingdom
Marla Hochfeld	Bristol Myers Squibb, New York, NY
Natalie Bowers	Genentech, San Francisco, CA
Rion Pendergrass	Genentech, San Francisco, CA
Jorge Esparza Gordillo	GlaxoSmithKline, Brentford, United Kingdom
Kirsi Auro	GlaxoSmithKline, Espoo, Finland
Dawn Waterworth	Janssen Research & Development, LLC, Spring House, PA
Fabiana Farias	Merck, Kenilworth, NJ
Kirsi Kalpala	Pfizer, New York, NY
Nan Bing	Pfizer, New York, NY
Xinli Hu	Pfizer, New York, NY
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	University of Gothenburg, Gothenburg, Sweden/Seinäjoki Central Hospital, Seinäjoki, Finland/Tampere University, Tampere, Finland
Terttu Harju	Northern Ostrobothnia Hospital District, Oulu, Finland
Riitta Lahesmaa	Hospital District of Southwest Finland, Turku, Finland
Nizar Smaoui	AbbVie, Chicago, IL
Alex Mackay	Astra Zeneca, Cambridge, United Kingdom
Glenda Lassi	Astra Zeneca, Cambridge, United Kingdom
Susan Eaton	Biogen, Cambridge, MA
Hubert Chen	Genentech, San Francisco, CA
Rion Pendergrass	Genentech, San Francisco, CA
Natalie Bowers	Genentech, San Francisco, CA
Joanna Betts	GlaxoSmithKline, Brentford, United Kingdom
Kirsi Auro	GlaxoSmithKline, Espoo, Finland
Rajashree Mishra	GlaxoSmithKline, Brentford, United Kingdom
Majd Mouded	Novartis, Basel, Switzerland
Debby Ngo	Novartis, Basel, Switzerland
Teemu Niiranen	Finnish Institute for Health and Welfare (THL), Helsinki, Finland
Felix Vaura	Finnish Institute for Health and Welfare (THL), Helsinki, Finland
Veikko Salomaa	Finnish Institute for Health and Welfare (THL), Helsinki, Finland
Kaj Metsärinne	Hospital District of Southwest Finland, Turku, Finland
Jenni Aittokallio	Hospital District of Southwest Finland, Turku, Finland
Mika Kähönen	Pirkanmaa Hospital District, Tampere, Finland
Jussi Hernesniemi	Pirkanmaa Hospital District, Tampere, Finland
Daniel Gordin	Hospital District of Helsinki and Uusimaa, Helsinki, 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
Timo Hiltunen	Hospital District of Helsinki and Uusimaa, Helsinki, Finland
Jari Laukkanen	Central Finland Health Care District, Jyväskylä, Finland

(continued on following page)

TABLE A1. FinnGen (continued)

Full Name	Affiliation
Amanda Elliott	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland; Broad Institute, Cambridge, MA; and Massachusetts General Hospital, Boston, MA
Mary Pat Reeve	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Sanni Ruotsalainen	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Benjamin Challis	Astra Zeneca, Cambridge, United Kingdom
Dirk Paul	Astra Zeneca, Cambridge, United Kingdom
Julie Hunkapiller	Genentech, San Francisco, CA
Natalie Bowers	Genentech, San Francisco, CA
Rion Pendergrass	Genentech, San Francisco, CA
Audrey Chu	GlaxoSmithKline, Brentford, United Kingdom
Kirsi Auro	GlaxoSmithKline, Espoo, Finland
Dermot Reilly	Janssen Research & Development, LLC, Boston, MA
Mike Mendelson	Novartis, Boston, MA
Jaakko Parkkinen	Pfizer, New York, NY
Melissa Miller	Pfizer, New York, NY
Tuomo Meretoja	Hospital District of Helsinki and Uusimaa, Helsinki, Finland
Heikki Joensuu	Hospital District of Helsinki and Uusimaa, Helsinki, Finland
Olli Carpén	Hospital District of Helsinki and Uusimaa, Helsinki, Finland
Johanna Mattson	Hospital District of Helsinki and Uusimaa, Helsinki, Finland
Eveliina Salminen	Hospital District of Helsinki and Uusimaa, Helsinki, Finland
Annika Auranen	Pirkanmaa Hospital District, Tampere, Finland
Peeter Karihtala	Northern Ostrobothnia Hospital District, Oulu, Finland
Päivi Auvinen	Northern Savo Hospital District, Kuopio, Finland
Klaus Elenius	Hospital District of Southwest Finland, Turku, Finland
Johanna Schleutker	Hospital District of Southwest Finland, Turku, Finland
Esa Pitkänen	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Nina Mars	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Mark Daly	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland; Broad Institute of MIT and Harvard; Massachusetts General Hospital
Relja Popovic	AbbVie, Chicago, IL
Jeffrey Waring	AbbVie, Chicago, IL
Bridget Riley-Gillis	AbbVie, Chicago, IL
Anne Lehtonen	AbbVie, Chicago, IL
Jennifer Schutzman	Genentech, San Francisco, CA
Julie Hunkapiller	Genentech, San Francisco, CA
Natalie Bowers	Genentech, San Francisco, CA
Rion Pendergrass	Genentech, San Francisco, CA
Diptee Kulkarni	GlaxoSmithKline, Brentford, United Kingdom
Kirsi Auro	GlaxoSmithKline, Espoo, Finland
Alessandro Porello	Janssen Research & Development, LLC, Spring House, PA
Andrey Loboda	Merck, Kenilworth, NJ
Heli Lehtonen	Pfizer, New York, NY
Stefan McDonough	Pfizer, New York, NY
Sauli Vuoti	Janssen-Cilag Oy, Espoo, Finland
Kai Kaarniranta	Northern Savo Hospital District, Kuopio, Finland
Joni A Turunen	Helsinki University Hospital and University of Helsinki, Helsinki, Finland; Eye Genetics Group, Folkhälsan Research Center, Helsinki, Finland
Terhi Ollila	Hospital District of Helsinki and Uusimaa, Helsinki, Finland
Hannu Uusitalo	Pirkanmaa Hospital District, Tampere, Finland
Juha Karjalainen	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland

(continued on following page)

TABLE A1. FinnGen (continued)

Full Name	Affiliation
Esa Pitkänen	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Mengzhen Liu	AbbVie, Chicago, IL
Heiko Runz	Biogen, Cambridge, MA
Stephanie Loomis	Biogen, Cambridge, MA
Erich Strauss	Genentech, San Francisco, CA
Natalie Bowers	Genentech, San Francisco, CA
Hao Chen	Genentech, San Francisco, CA
Rion Pendergrass	Genentech, San Francisco, CA
Kaisa Tasanen	Northern Ostrobothnia Hospital District, Oulu, Finland
Laura Huilaja	Northern Ostrobothnia Hospital District, Oulu, Finland
Katariina Hannula-Jouppi	Hospital District of Helsinki and Uusimaa, Helsinki, Finland
Teea Salmi	Pirkanmaa Hospital District, Tampere, Finland
Sirkku Peltonen	Hospital District of Southwest Finland, Turku, Finland
Leena Koulu	Hospital District of Southwest Finland, Turku, Finland
Nizar Smaoui	AbbVie, Chicago, IL
Fedik Rahimov	AbbVie, Chicago, IL
Anne Lehtonen	AbbVie, Chicago, IL
David Choy	Genentech, San Francisco, CA
Rion Pendergrass	Genentech, San Francisco, CA
Dawn Waterworth	Janssen Research & Development, LLC, Spring House, PA
Kirsi Kalpala	Pfizer, New York, NY
Ying Wu	Pfizer, New York, NY
Pirkko Pussinen	Hospital District of Helsinki and Uusimaa, Helsinki, Finland
Aino Salminen	Hospital District of Helsinki and Uusimaa, Helsinki, Finland
Tuula Salo	Hospital District of Helsinki and Uusimaa, Helsinki, Finland
David Rice	Hospital District of Helsinki and Uusimaa, Helsinki, Finland
Pekka Nieminen	Hospital District of Helsinki and Uusimaa, Helsinki, Finland
Ulla Palotie	Hospital District of Helsinki and Uusimaa, Helsinki, Finland
Maria Siponen	Northern Savo Hospital District, Kuopio, Finland
Liisa Suominen	Northern Savo Hospital District, Kuopio, Finland
Päivi Mäntylä	Northern Savo Hospital District, Kuopio, Finland
Ulvi Gursoy	Hospital District of Southwest Finland, Turku, Finland
Vuokko Anttonen	Northern Ostrobothnia Hospital District, Oulu, Finland
Kirsi Sipilä	Research Unit of Oral Health Sciences Faculty of Medicine, University of Oulu, Oulu, Finland; Medical Research Center, Oulu, Oulu University Hospital and University of Oulu, Oulu, Finland
Rion Pendergrass	Genentech, San Francisco, CA
Hannele Laivuori	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Venla Kurra	Pirkanmaa Hospital District, Tampere, Finland
Laura Kotaniemi-Talonen	Pirkanmaa Hospital District, Tampere, Finland
Oskari Heikinheimo	Hospital District of Helsinki and Uusimaa, Helsinki, Finland
Ilkka Kalliala	Hospital District of Helsinki and Uusimaa, Helsinki, Finland
Lauri Aaltonen	Hospital District of Helsinki and Uusimaa, Helsinki, Finland
Varpu Jokimaa	Hospital District of Southwest Finland, Turku, Finland
Johannes Kettunen	Northern Ostrobothnia Hospital District, Oulu, Finland
Marja Vääräsmäki	Northern Ostrobothnia Hospital District, Oulu, Finland
Outi Uimari	Northern Ostrobothnia Hospital District, Oulu, Finland
Laure Morin-Papunen	Northern Ostrobothnia Hospital District, Oulu, Finland
Maarit Niinimäki	Northern Ostrobothnia Hospital District, Oulu, Finland
Terhi Piltonen	Northern Ostrobothnia Hospital District, Oulu, Finland
Katja Kivinen	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland

(continued on following page)

TABLE A1. FinnGen (continued)

Full Name	Affiliation
Elisabeth Widen	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Taru Tukiainen	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Mary Pat Reeve	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Mark Daly	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland; Broad Institute of MIT and Harvard; Massachusetts General Hospital
Niko Välimäki	University of Helsinki, Helsinki, Finland
Eija Laakkonen	University of Jyväskylä, Jyväskylä, Finland
Jaakko Tyrmi	University of Oulu, Oulu, Finland/University of Tampere, Tampere, Finland
Heidi Silven	University of Oulu, Oulu, Finland
Eeva Sliz	University of Oulu, Oulu, Finland
Riikka Arffman	University of Oulu, Oulu, Finland
Susanna Savukoski	University of Oulu, Oulu, Finland
Triin Laisk	Estonian biobank, Tartu, Estonia
Natalia Pujol	Estonian biobank, Tartu, Estonia
Mengzhen Liu	AbbVie, Chicago, IL
Bridget Riley-Gillis	AbbVie, Chicago, IL
Rion Pendergrass	Genentech, San Francisco, CA
Janet Kumar	GlaxoSmithKline, Collegeville, PA
Kirsi Auro	GlaxoSmithKline, Espoo, Finland
Iiris Hovatta	University of Helsinki, Finland
Chia-Yen Chen	Biogen, Cambridge, MA
Erkki Isometsä	Hospital District of Helsinki and Uusimaa, Helsinki, Finland
Kumar Veerapen	Broad Institute, Cambridge, MA
Hanna Ollila	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Jaana Suvisaari	Finnish Institute for Health and Welfare (THL), Helsinki, Finland
Thomas Damm Als	Aarhus University, Denmark
Antti Mäkitie	Department of Otorhinolaryngology—Head and Neck Surgery, University of Helsinki and Helsinki University Hospital, Helsinki, Finland
Argyro Bizaki-Vallaskangas	Pirkanmaa Hospital District, Tampere, Finland
Sanna Toppila-Salmi	University of Helsinki, Finland
Tytti Willberg	Hospital District of Southwest Finland, Turku, Finland
Elmo Saarentaus	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Antti Aarnisalo	Hospital District of Helsinki and Uusimaa, Helsinki, Finland
Eveliina Salminen	Hospital District of Helsinki and Uusimaa, Helsinki, Finland
Elisa Rahikkala	Northern Ostrobothnia Hospital District, Oulu, Finland
Johannes Kettunen	Northern Ostrobothnia Hospital District, Oulu, Finland
Kristiina Aittomäki	Department of Medical Genetics, Helsinki University Central Hospital, Helsinki, Finland
Fredrik Åberg	Transplantation and Liver Surgery Clinic, Helsinki University Hospital, Helsinki University, Helsinki, Finland
Mitja Kurki	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland; Broad Institute, Cambridge, MA
Samuli Ripatti	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Mark Daly	Institute for Molecular Medicine, Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland; Broad Institute of MIT and Harvard; Massachusetts General Hospital
Juha Karjalainen	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Aki Havulinna	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland; Finnish Institute for Health and Welfare (THL), Helsinki, Finland
Juha Mehtonen	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Priit Palta	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Shabbeer Hassan	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Pietro Della Briotta Parolo	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Wei Zhou	Broad Institute, Cambridge, MA

(continued on following page)

TABLE A1. FinnGen (continued)

Full Name	Affiliation
Mutaamba Maasha	Broad Institute, Cambridge, MA
Kumar Veerapen	Broad Institute, Cambridge, MA
Shabbeer Hassan	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Susanna Lemmelä	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Manuel Rivas	University of Stanford, Stanford, CA
Mari E. Niemi	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Aarno Palotie	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Aoxing Liu	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Arto Lehisto	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Andrea Ganna	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Vincent Llorens	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Hannele Laivuori	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Taru Tukiainen	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Mary Pat Reeve	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Henrike Heyne	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Nina Mars	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Joel Rämö	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Elmo Saarentaus	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Hanna Ollila	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Rodos Rodosthenous	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Satu Strausz	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Tuula Palotie	University of Helsinki and Hospital District of Helsinki and Uusimaa, Helsinki, Finland
Kimmo Palin	University of Helsinki, Helsinki, Finland
Javier Garcia-Tabuenca	University of Tampere, Tampere, Finland
Harri Siirtola	University of Tampere, Tampere, Finland
Tuomo Kiiskinen	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Jiwoo Lee	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland; Broad Institute, Cambridge, MA
Kristin Tsuo	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland; Broad Institute, Cambridge, MA
Amanda Elliott	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland; Broad Institute, Cambridge, MA and Massachusetts General Hospital, Boston, MA
Kati Kristiansson	THL Biobank/Finnish Institute for Health and Welfare (THL), Helsinki, Finland
Mikko Arvas	Finnish Red Cross Blood Service/Finnish Hematology Registry and Clinical Biobank, Helsinki, Finland
Kati Hyvärinen	Finnish Red Cross Blood Service, Helsinki, Finland
Jarmo Ritari	Finnish Red Cross Blood Service, Helsinki, Finland
Olli Carpén	Helsinki Biobank/Helsinki University and Hospital District of Helsinki and Uusimaa, Helsinki
Johannes Kettunen	Northern Finland Biobank Borealis/University of Oulu/Northern Ostrobothnia Hospital District, Oulu, Finland
Katri Pylkäs	University of Oulu, Oulu, Finland
Eeva Sliz	University of Oulu, Oulu, Finland
Minna Karjalainen	University of Oulu, 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	University of Eastern Finland, Kuopio, Finland
Arto Mannermaa	Biobank of Eastern Finland/University of Eastern Finland/Northern Savo Hospital District, Kuopio, Finland
Eija Laakkonen	University of Jyväskylä, Jyväskylä, Finland
Nina Pitkänen	Auria Biobank/University of Turku/Hospital District of Southwest Finland, Turku, Finland
Samuel Lessard	Translational Sciences, Sanofi R&D, Framingham, MA
Clément Chatelain	Translational Sciences, Sanofi R&D, Framingham, MA
Perttu Terho	Auria Biobank/University of Turku/Hospital District of Southwest Finland, Turku, Finland

(continued on following page)

TABLE A1. FinnGen (continued)

Full Name	Affiliation
Sirpa Soini	THL Biobank/Finnish Institute for Health and Welfare (THL), Helsinki, Finland
Jukka Partanen	Finnish Red Cross Blood Service/Finnish Hematology Registry and Clinical Biobank, Helsinki, Finland
Eero Punkka	Helsinki Biobank/Helsinki University and Hospital District of Helsinki and Uusimaa, Helsinki
Raisa Serpi	Northern Finland Biobank Borealis/University of Oulu/Northern Ostrobothnia Hospital District, Oulu, Finland
Sanna Siltanen	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
Teijo Kuopio	Central Finland Biobank/University of Jyväskylä/Central Finland Health Care District, Jyväskylä, Finland
Anu Jalanko	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Huei-Yi Shen	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Risto Kajanne	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Mervi Aavikko	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Mitja Kurki	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland; Broad Institute, Cambridge, MA
Juha Karjalainen	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Pietro Della Briotta Parolo	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Arto Lehisto	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Juha Mehtonen	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Wei Zhou	Broad Institute, Cambridge, MA
Masahiro Kanai	Broad Institute, Cambridge, MA
Mutaamba Maasha	Broad Institute, Cambridge, MA
Kumar Veerapen	Broad Institute, Cambridge, MA
Hannele Laivuori	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Aki Havulinna	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland; Finnish Institute for Health and Welfare (THL), Helsinki, Finland
Susanna Lemmelä	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Tuomo Kiiskinen	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
L. Elisa Lahtela	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Mari Kaunisto	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Elina Kilpeläinen	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Timo P. Sipilä	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Oluwaseun Alexander Dada	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Awaisa Ghazal	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Anastasia Kytölä	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Rigbe Weldatsadik	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Kati Donner	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Timo P. Sipilä	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Anu Loukola	Helsinki Biobank/Helsinki University and Hospital District of Helsinki and Uusimaa, Helsinki
Päivi Laiho	THL Biobank/Finnish Institute for Health and Welfare (THL), Helsinki, Finland
Tuuli Sistonen	THL Biobank/Finnish Institute for Health and Welfare (THL), Helsinki, Finland
Essi Kaiharju	THL Biobank/Finnish Institute for Health and Welfare (THL), Helsinki, Finland
Markku Laukkanen	THL Biobank/Finnish Institute for Health and Welfare (THL), Helsinki, Finland
Elina Järvensivu	THL Biobank/Finnish Institute for Health and Welfare (THL), Helsinki, Finland
Sini Lähteenmäki	THL Biobank/Finnish Institute for Health and Welfare (THL), Helsinki, Finland
Lotta Männikkö	THL Biobank/Finnish Institute for Health and Welfare (THL), Helsinki, Finland
Regis Wong	THL Biobank/Finnish Institute for Health and Welfare (THL), Helsinki, Finland
Auli Toivola	THL Biobank/Finnish Institute for Health and Welfare (THL), Helsinki, Finland
Minna Brunfeldt	THL Biobank/Finnish Institute for Health and Welfare (THL), Helsinki, Finland
Hannele Mattsson	THL Biobank/Finnish Institute for Health and Welfare (THL), Helsinki, Finland
Kati Kristiansson	THL Biobank/Finnish Institute for Health and Welfare (THL), Helsinki, Finland
Susanna Lemmelä	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland

(continued on following page)

TABLE A1. FinnGen (continued)

Full Name	Affiliation
Sami Koskelainen	THL Biobank/Finnish Institute for Health and Welfare (THL), Helsinki, Finland
Tero Hiekkalinna	THL Biobank/Finnish Institute for Health and Welfare (THL), Helsinki, Finland
Teemu Paajanen	THL Biobank/Finnish Institute for Health and Welfare (THL), Helsinki, Finland
Priit Palta	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Kalle Pärn	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Mart Kals	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Shuang Luo	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Vishal Sinha	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Tarja Laitinen	Pirkanmaa Hospital District, Tampere, Finland
Mary Pat Reeve	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Marianna Niemi	University of Tampere, Tampere, Finland
Kumar Veerapen	Broad Institute, Cambridge, MA
Harri Siirtola	University of Tampere, Tampere, Finland
Javier Gracia-Tabuenca	University of Tampere, Tampere, Finland
Mika Helminen	University of Tampere, Tampere, Finland
Tiina Luukkaala	University of Tampere, Tampere, Finland
Iida Vähätalo	University of Tampere, Tampere, Finland
Jyrki Pitkänen	Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
Marco Hautalahti	Finnish Biobank Cooperative—FINBB
Johanna Mäkelä	Finnish Biobank Cooperative—FINBB
Sarah Smith	Finnish Biobank Cooperative—FINBB
Tom Southerington	Finnish Biobank Cooperative—FINBB