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ORIGINAL ARTICLE

Polygenic Risk Score for Low-Density Lipoprotein Cholesterol Is Associated With Risk of Ischemic Heart Disease and Enriches for Individuals With Familial Hypercholesterolemia

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BACKGROUND: The clinical implications of a polygenic risk score (PRS) for LDL-C (low-density lipoprotein cholesterol) are not well understood, both within the general population and individuals with familial hypercholesterolemia (FH).

METHODS: We developed the LDL-C PRS using Least Absolute Shrinkage and Selection Operator regression in 377 286 White British participants from UK Biobank and tested its association with LDL-C according to FH variant carrier status in another 41 748 whole-exome sequenced individuals. Next, we tested for an enrichment of FH variant carriers among individuals with severe hypercholesterolemia and low LDL-C PRS. Last, we contrasted the effect of the LDL-C PRS, measured LDL-C and FH variant carrier status on risk of ischemic heart disease among 3010 cases and 38 738 controls.

RESULTS: Among the 41 748 whole-exome sequenced White British individuals, 1-SD increase in the LDL-C PRS was associated with elevated LDL-C among both FH variant carriers (0.34 [95% CI, 0.22–0.47] mmol/L) and noncarriers (0.42 [95% CI, 0.42–0.43] mmol/L). Among individuals with severe hypercholesterolemia, FH variant carriers were enriched in those with a low LDL-C PRS (odds ratio, 2.20 [95% CI, 1.66–2.71] per SD). Each SD increase in the LDL-C PRS was associated with risk of ischemic heart disease to the comparable magnitude as measured LDL-C (odds ratio, 1.24 [95% CI, 1.20–1.29] and odds ratio, 1.15 [95% CI, 1.09–1.23], respectively). The LDL-C PRS was not strongly associated with other traditional ischemic heart disease risk factors.

CONCLUSIONS: An LDL-C PRS could be used to identify individuals with a higher probability of harboring FH variants. The association between ischemic heart disease and the LDL-C PRS was comparable to measured LDL-C, likely because the PRS reflects lifetime exposure to LDL-C levels.

Key Words: cholesterol ■ epidemiology ■ genetics ■ heart diseases ■ hypercholesterolemia

Cardiovascular disease (CVD) is the leading cause of premature mortality worldwide.[1] Important improvements in the primary and secondary prevention of CVD have been achieved through the identification and treatment of individuals with increased LDL-C (low-density lipoprotein cholesterol), as LDL-C level has been shown to be strongly associated with the risk of ischemic heart disease (IHD).[2,3] Most clinical efforts to identify individuals with genetically elevated LDL-C have focused on identifying individuals in the general population who have rare but penetrant alleles leading to familial hypercholesterolemia (FH).[4–7] However, large-scale genome-wide association studies have enabled a more precise understanding of the common genetic

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Nonstandard Abbreviations and Acronyms

CVD	cardiovascular disease
FH	familial hypercholesterolemia
GWI	genome-wide imputed
IHD	ischemic heart disease
LDL-C	low-density lipoprotein cholesterol
OR	odds ratio
PRS	polygenic risk score
WES	whole-exome sequenced

variants that influence LDL-C levels, which can now be summed together through polygenic risk scores (PRSs) that explain a relatively large proportion of the variance in common traits and diseases.[8]

Talmud et al[9] and Natarajan et al[10] separately showed that monogenic and polygenic causes could both lead to severe hypercholesterolemia (LDL-C ≥4.9 mmol/L) or clinical FH. Combined with other recent studies[6,7,11] demonstrating a role for polygenic risk, these findings suggest that an important proportion of individuals with clinical FH may have a polygenic cause, and their genetic predisposition would be missed through sequencing focused on only *LDLR*, *APOB*, and *PCSK9* genes. In addition, Trinder et al[12] recently found that both monogenic and polygenic causes of hypercholesterolemia may impose additional risks of CVD.

We posit that an LDL-C PRS could help to identify FH variant carriers among individuals with severe hypercholesterolemia, as individuals with severe hypercholesterolemia but a low polygenic risk for LDL-C would be more likely to have a monogenic cause of hypercholesterolemia, such as FH variants.[13] Furthermore, an LDL-C PRS would be more likely to reflect a lifetime exposure to elevated LDL-C than LDL-C measured at one time point and could potentially capture risk of IHD independently of LDL-C through pleiotropic pathways. Last, an LDL-C PRS may help to explain the variable penetrance of FH pathogenic variants.

Here, we describe an improved LDL-C PRS generated from UK Biobank, which is strongly associated with LDL-C and IHD risk, and demonstrate the enrichment of FH patients among individuals with severe hypercholesterolemia and a low LDL-C PRS. We, therefore, provide insights into the possible roles that an LDL-C PRS may eventually play in clinical care.

METHODS

The study methods are provided in the Data Supplement. The overall study design is presented in Figure 1. The UK Biobank was approved by the North West Multicentre Research Ethics Committee, and all participants gave written and informed consent before participation. All relevant summary-level data are within the article and the Data Supplement. All other relevant underlying individual-level data will be returned to UK Biobank in accordance with the signed Material Transfer Agreement.

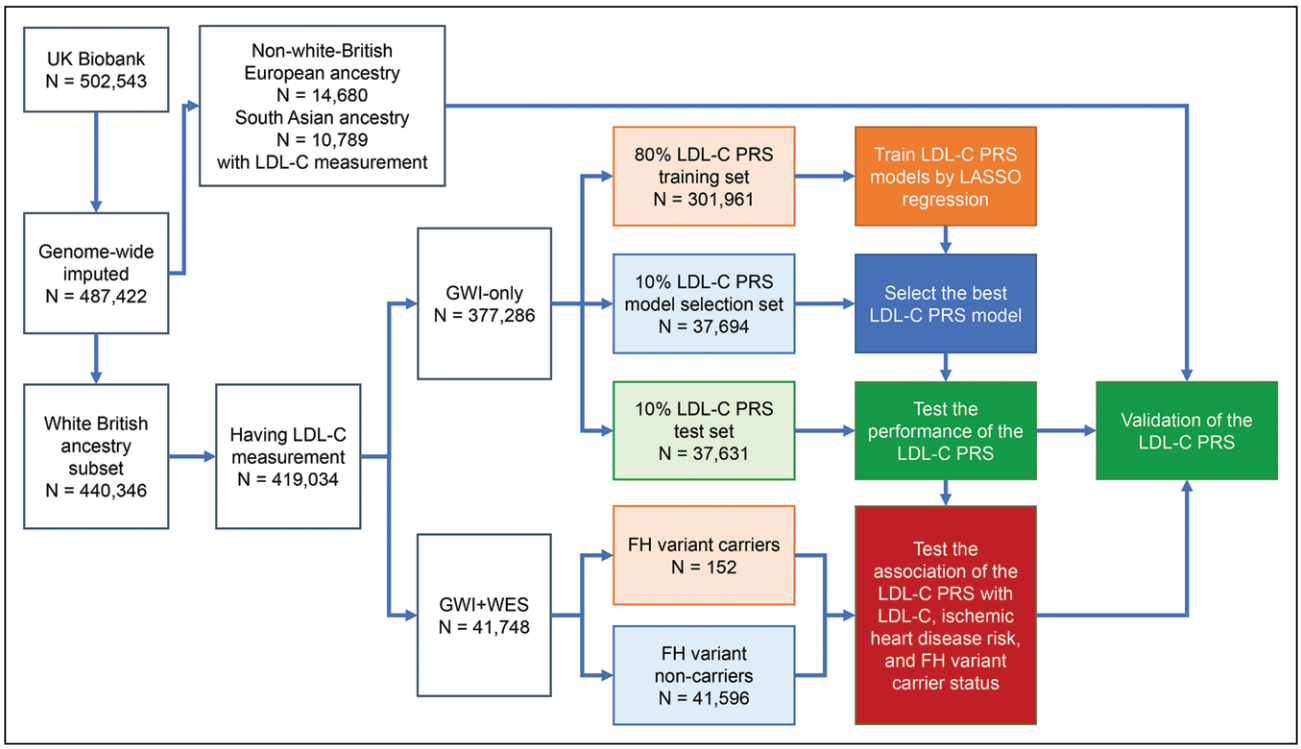

Figure 1. Study design.
FH indicates familial hypercholesterolemia; GWI, genome-wide imputed; LDL-C, low-density lipoprotein cholesterol; PRS, polygenic risk score; and WES, whole-exome sequenced.

UK Biobank will then make this individual-level data available to researchers in accordance with their data access policies.

RESULTS

Development of the Polygenic Predictor for LDL-C

The 377 326 genome-wide imputed (GWI-only) White British UK Biobank participants with LDL-C measurement were randomly assigned into 80% training (n=301 961), 10% model selection (n=37 694), and 10% validation (n=37 631) sets. The characteristics of the individuals in the PRS training, model selection, and validation subsets were shown in Table I in the Data Supplement. Before the subsequent analyses, directly measured LDL-C levels were adjusted based on cholesterol-lowering medication use (Table II in the Data Supplement). Least Absolute Shrinkage and Selection Operator regression generated 100 candidate PRS models from the training set. The PRS model with the lowest rooted mean square error in the model selection set included 8367 activated single-nucleotide polymorphisms, which explained 21.5% (95% CI, 20.7%–22.2%) of the variance in LDL-C level in the independent validation set.

Polygenic Prediction of LDL-C Level

This PRS was then used to predict LDL-C level for the 41 748 GWI and whole-exome sequenced (GWI+WES) individuals, in which it explained 21.1% (95% CI, 21.4%–21.8%) of the variance in LDL-C level (Table 1, Figure I in the Data Supplement). The LDL-C PRS was standardized to have a mean of 0 and an SD of 1 in the 41 748 GWI+WES individuals for downstream analyses.

FH Variants in GWI+WES Individuals

Among the 41 748 GWI+WES individuals, we found 75 FH-associated variants, including 15 loss-of-function variants in *LDLR*, 47 deleterious missense variants in *LDLR*, and 13 additional variants from ClinVar.[14] These variants were not present in the GWI-only data set and thus were not present in the LDL-C PRS. Detailed information on the identified FH variants is provided in Table III in the Data Supplement. Among the 41 748 GWI+WES individuals, 152 (0.4%) individuals were identified to carry at least one FH variant. Table 2 shows the characteristics of FH variant carriers and noncarriers.

Table 1. Performance of the LDL-C PRS in Different Cohorts

Cohort	Sample size	r^{2*}	95% CI
Model selection	37 694	0.213	0.205–0.220
Validation	37 631	0.215	0.207–0.222
Whole-exome sequenced	41 748	0.211	0.204–0.218
Non-White British European	12 115†	0.186	0.174–0.199
South Asian	7916†	0.139	0.125–0.154

LDL-C indicates low-density lipoprotein cholesterol; and PRS, polygenic risk score.

*r^2: variance explained, the square of Pearson correlation.

†No. of individuals who did not take any cholesterol-lowering medication.

Relationship Between LDL-C, LDL-C PRS, and FH Variant Carrier Status

The distribution of the LDL-C PRS and LDL-C by FH variant carriers and noncarriers is presented in Figure II in the Data Supplement. As expected, we observed little difference in LDL-C PRS when comparing FH variant carriers to noncarriers. The mean LDL-C level of FH variant carriers was higher than noncarriers by 0.86 (95% CI, 0.72–1.01) mmol/L adjusted for age and sex, and the difference (0.87 [95% CI, 0.74–0.99] mmol/L) persisted after adjusting for the LDL-C PRS.

As the decile of the LDL-C PRS increased, LDL-C level increased to a clinically relevant degree among both FH variant carriers and noncarriers (Figure 2). One SD increase in the LDL-C PRS was associated with 0.34 (95% CI, 0.22–0.47) mmol/L and 0.42 (95% CI, 0.42–0.43) mmol/L increase in LDL-C level among FH variant carriers and noncarriers, respectively (Figure III in the Data Supplement). There was no appreciable difference (−0.08 [95% CI, −0.21 to 0.05] mmol/L) in the LDL-C PRS's association with LDL-C between FH variant carriers and noncarriers. These results suggest that the LDL-C PRS and FH variants have independent effect on LDL-C.

Table 2. Basis Characteristics of FH Variant Carriers and Noncarriers

	FH variant carriers (n=152)	FH variant noncarriers (n=41 596)
Age when attending assessment center, y	57.86±7.78*	56.87±7.92
Female	85 (55.9%)†	22,577 (54.3%)
LDL-C level, mmol/L, before adjustment	3.73±1.21	3.55±0.86
LDL-C level, mmol/L, after adjustment	4.72±1.55	3.83±0.91
Body mass index, kg/m^2	27.64±5.10	27.39±4.76
Systolic blood pressure, mm Hg	134.16±17.86	134.68±18.14
Type 2 diabetes	9 (5.9%)	1726 (4.1%)
Smoking (ever)	59 (38.8%)	18,773 (45.1%)
Smoking (current)	10 (6.6%)	36,68 (8.8%)
Cholesterol-lowering medication	73 (48.0%)	7593 (18.3%)

FH indicates familial hypercholesterolemia; and LDL-C, low-density lipoprotein cholesterol.

*Plus–minus values are means±SD.

†N (%) values are numbers of individuals (percentages).

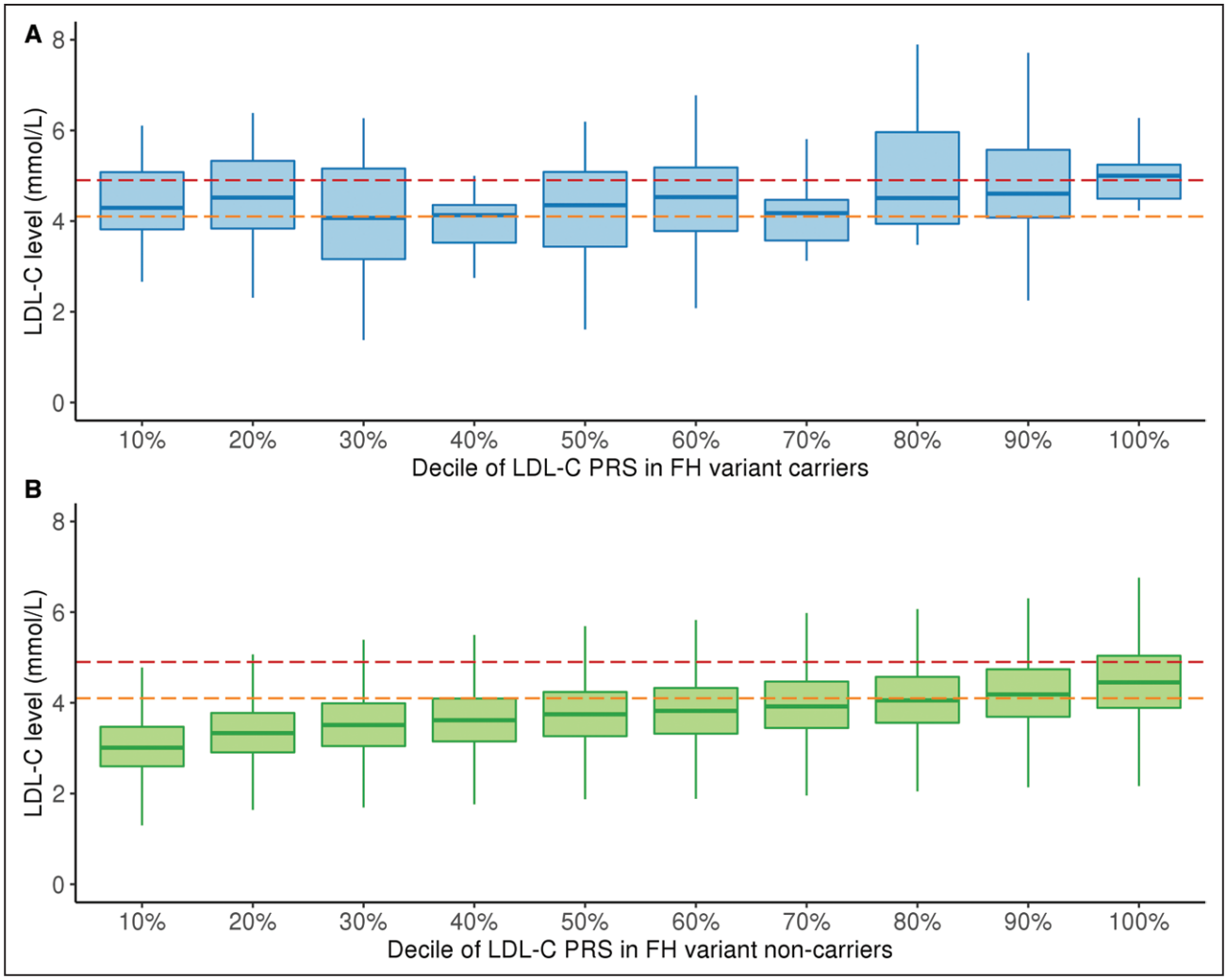

Figure 2. Distribution of LDL-C (low-density lipoprotein cholesterol) level according to the LDL-C polygenic risk score (PRS) deciles in familial hypercholesterolemia (FH) variant carriers and noncarriers.
A, distribution of LDL-C level by LDL-C PRS deciles in FH variant carriers. **B**, distribution of LDL-C level by LDL-C PRS deciles in FH variant noncarriers. The orange and red dotted lines represent LDL-C=4.1 and LDL-C=4.9 mmol/L, respectively.

FH Variant Carrier Status Predicted by LDL-C PRS and Severe Hypercholesterolemia

There were 60 (39.5%) FH variant carriers and 4588 (11.0%) noncarriers in the GWI+WES data set that had severe hypercholesterolemia. FH variant carriers were more likely to be found among individuals with severe hypercholesterolemia (odds ratio [OR], 7.50 [95% CI, 5.32–10.50]). Among individuals with severe hypercholesterolemia, 1-SD decrease in the LDL-C PRS was associated with increased odds of harboring FH variants (OR, 2.20 [95% CI, 1.66–2.71]), and such association was not observed in individuals without severe hypercholesterolemia (Table 3, Figure 3). In particular, among severe hypercholesterolemia patients, individuals with an LDL-C PRS 2-SD lower than the population mean were predicted to have 21-fold higher probability of carrying FH variants than individuals with an LDL-C PRS 2-SD higher than the population mean.

Association of LDL-C PRS, FH Variant Carrier Status, LDL-C With Risk of IHD

There were 3010 (7.2%) IHD cases, including 1110 (2.7%) incident cases, among the 41 748 GWI+WES individuals. The proportion of the population experiencing an IHD diagnosis increased across percentiles of the LDL-C PRS (Figure 4). There were 26 (17.1%) FH variant carriers that experienced a prevalent or incident IHD, compared with 2984 (7.2%) IHD cases among FH variant noncarriers. An increase of IHD incidence across LDL-C percentiles was also observed.

One SD increase in the LDL-C PRS was associated with 24% higher odds (OR, 1.24 [95% CI, 1.20–1.29]) of IHD (Figure 4). Individuals in the highest percentile of the LDL-C PRS had 1.76-fold higher odds (OR, 1.76 [95% CI, 1.29–2.35]) of IHD than the remainder of the population. FH variant carriers, on average, had 2.67-fold higher odds (OR, 2.67 [95% CI, 1.71–4.01]) of having IHD than

Table 3. Predicted Probability of Carrying FH Variants by LDL-C PRS and Severe Hypercholesterolemia

LDL-C PRS*	Predicted probability of carrying FH variants (95% CI)	
	LDL-C≥4.9 mmol/L	LDL-C<4.9 mmol/L
−3	16.9% (7.3%–34.5%)	0.3% (0.1%–0.5%)
−2	8.5% (4.5%–15.5%)	0.3% (0.2%–0.4%)
−1	4.0% (2.6%–6.1%)	0.3% (0.2%–0.4%)
0	1.9% (1.4%–2.5%)	0.3% (0.2%–0.3%)
1	0.9% (0.6%–1.3%)	0.2% (0.2%–0.4%)
2	0.4% (0.2%–0.7%)	0.2% (0.1%–0.4%)
3	0.2% (0.1%–0.4%)	0.2% (0.1%–0.5%)

FH indicates familial hypercholesterolemia; LDL-C, low-density lipoprotein cholesterol; and PRS, polygenic risk score.

*The LDL-C PRS has been standardized to have a mean of 0 and an SD of 1.

noncarriers. One SD increase in LDL-C was associated with 15% increased odds (OR, 1.15 [95% CI, 1.09–1.23]) of IHD (Table 4). After adjusting for LDL-C level and other IHD risk factors (age, sex, systolic blood pressure, body mass index, smoking, and type 2 diabetes), 1-SD increase in the LDL-C PRS remained associated with 10% higher odds (OR, 1.10 [95% CI, 1.03–1.18]) of incident IHD. The LDL-C PRS showed no obvious association with other traditional IHD risk factors other than the blood lipid traits (Table 5). The results provide evidence that the LDL-C PRS may capture IHD risks that are partly independent of LDL-C and traditional risk factors.

After removing 2119 individuals with IHD diagnosis at baseline and 6043 individuals on cholesterol-lowering medications, 619 incident IHD cases and 32 967 controls remained. Within this subgroup, 1-SD increase in the LDL-C PRS and LDL-C level was associated with 1.13 (95% CI, 1.02–1.24) -fold and 1.19 (95% CI, 1.07–1.32) -fold increased odds of incident IHD, respectively. This finding decreases the probability of reverse causation, where the onset of IHD could influence LDL-C level through lifestyle and pharmacological interventions.

Among FH variant noncarriers, the odds of prevalent or incident IHD increased by 25% (OR, 1.25 [95% CI, 1.20–1.30]) per 1-SD increase in the LDL-C PRS. The association between the LDL-C PRS and IHD among FH variant carriers was not conclusive (OR, 0.73 [95% CI, 0.48–1.11]). When restricting to incident IHD, 1-SD increase in the LDL-C PRS was associated with 1.08 (95% CI, 1.02–1.17) -fold increased odds of incident IHD among FH variant noncarriers; the association between the LDL-C PRS and IHD incidence among FH variant carriers remained inconclusive (OR, 2.68 [95% CI, 0.73–9.91]).

Validation of the LDL-C PRS in Other Ancestries

Among the 12 115 non-White British European population and 7916 South Asian population in the UK Biobank without self-reported cholesterol-lowering medication use, the variance in LDL-C level explained by the LDL-C

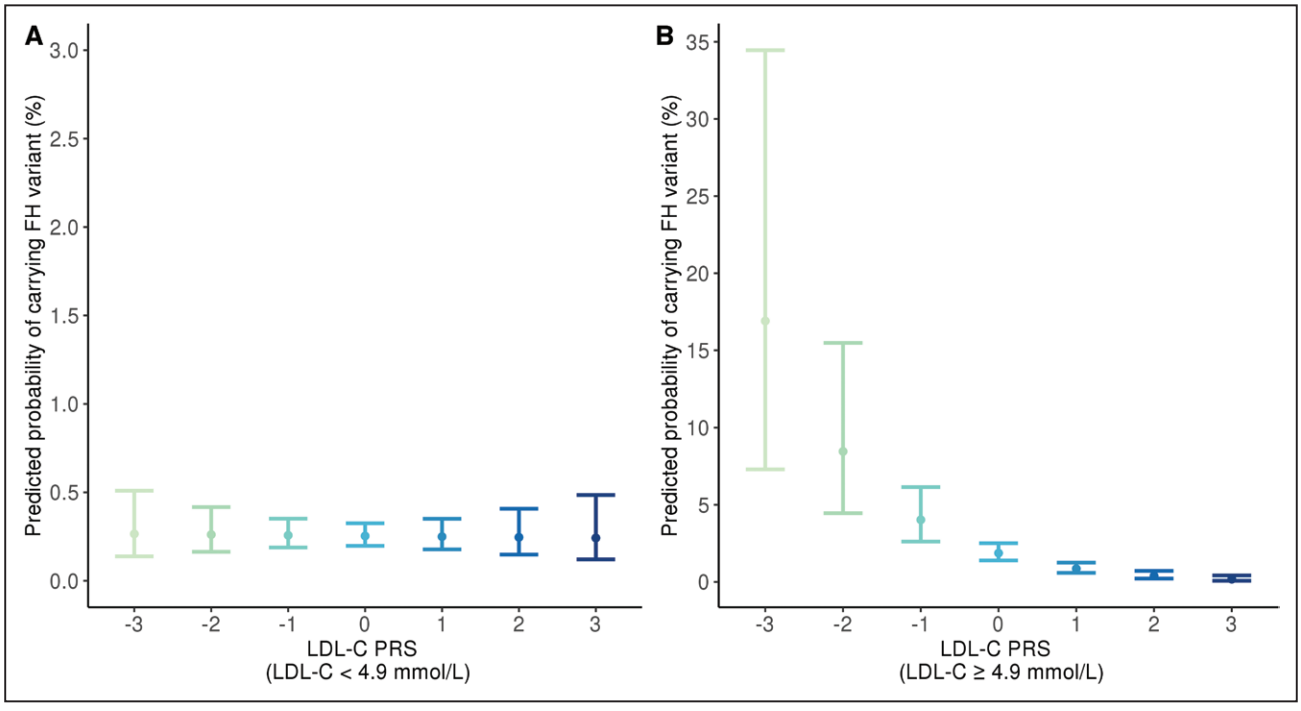

Figure 3. Predicted probability of carrying familial hypercholesterolemia (FH) variant according to the LDL-C (low-density lipoprotein cholesterol) polygenic risk score (PRS) and severe hypercholesterolemia (LDL-C≥4.9 mmol/L) status.
A, predicted probability of carrying FH variant by LDL-C PRS among individuals without severe hypercholesterolemia. **B**, predicted probability of carrying FH variant by LDL-C PRS among severe hypercholesterolemia patients. The LDL-C PRS has been standardized to have a mean of 0 and an SD of 1. Error bars represent 95% CIs.

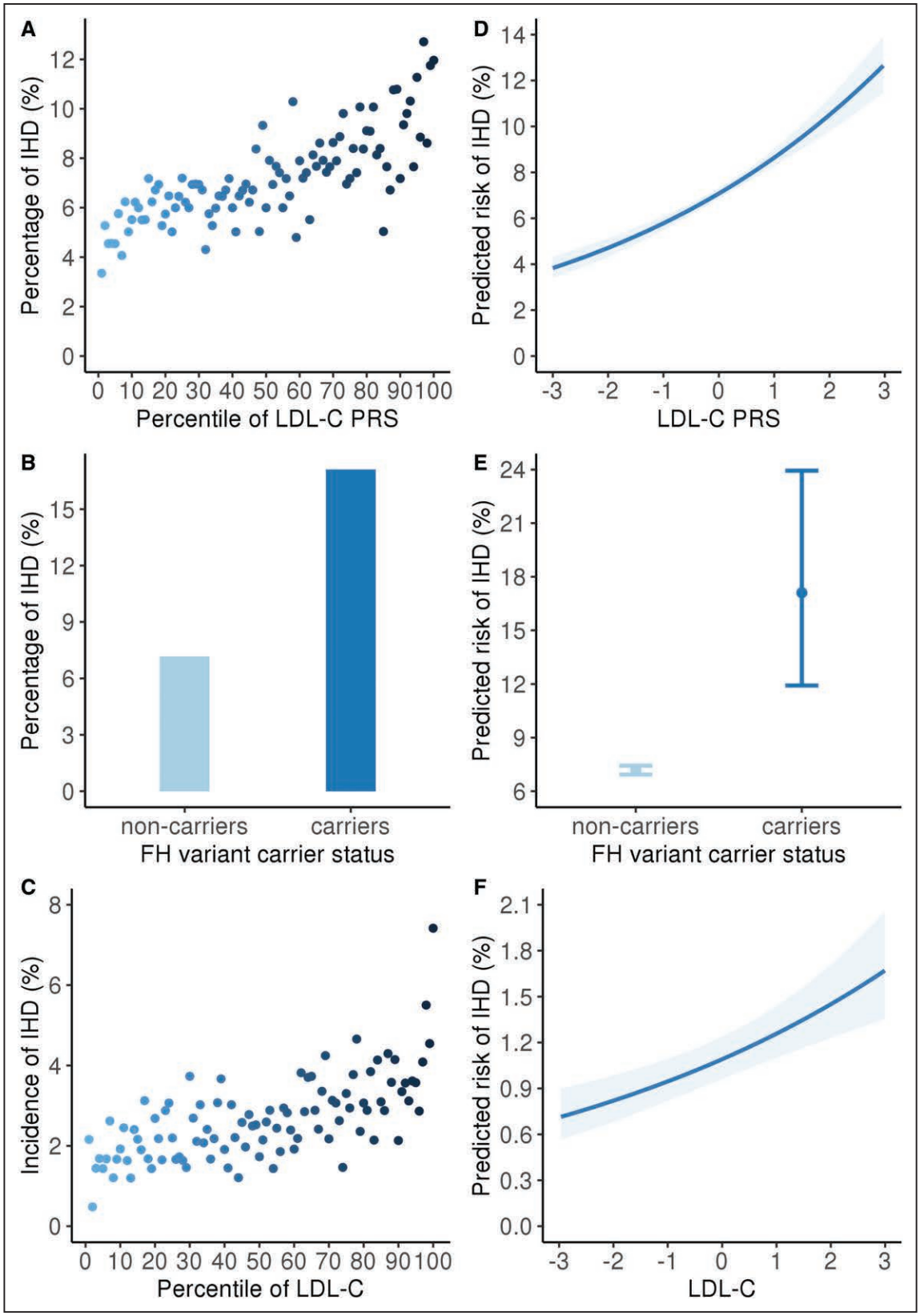

Figure 4. Risk gradient for ischemic heart disease (IHD) according to the LDL-C (low-density lipoprotein cholesterol) polygenic risk score (PRS), familial hypercholesterolemia (FH) variant status, and LDL-C level.
A, Observed percentage of prevalent or incident IHD according to the LDL-C PRS percentiles. **B**, Observed percentage of prevalent or incident IHD according FH variant carrier status. **C**, Observed incidence of IHD according to LDL-C percentiles. **D**, Predicted risk of IHD by the LDL-C PRS. **E**, Predicted risk of IHD by the FH variant carrier status. **F**, Predicted risk of IHD by LDL-C. LDL-C PRS and LDL-C were standardized to have a mean of 0 and an SD of 1. Ribbons and error bars represent 95% CIs.

Table 4. Association Between LDL-C PRS, FH Variant Carrier Status, LDL-C, and IHD Risk

Risk factor	Odds ratio*	95% CI
LDL-C PRS	1.24	1.20–1.29
FH variant carrier status	2.67	1.71–4.01
LDL-C	1.15	1.09–1.23

FH indicates familial hypercholesterolemia; IHD, ischemic heart disease; LDL-C, low-density lipoprotein cholesterol; and PRS, polygenic risk score.

*Odds ratios of IHD were calculated per SD increase for LDL-C PRS and LDL-C.

PRS was 18.6% (95% CI, 17.4%–19.9%) and 13.9% (95% CI, 12.5%–15.4%), respectively.

Among the 14 680 non-White British European individuals, 1-SD increase in the LDL-C PRS was associated with a 0.39 (95% CI, 0.38–0.41) mmol/L increase in LDL-C. A 1.23 (95% CI, 1.15–1.32) -fold and 1.25 (95% CI, 1.14–1.37) -fold increased odds of having IHD was associated with 1-SD increase in the LDL-C PRS and LDL-C, respectively. The LDL-C PRS remained associated with IHD incidence (OR, 1.17 [95% CI, 1.04–1.31]) after adjusting for measured LDL-C and other traditional risk factors.

Among the 10 789 South Asian UK Biobank participants, LDL-C on average increased by 0.32 (95% CI, 0.30–0.34) mmol/L per 1-SD increase in the LDL-C PRS. One SD increase in the LDL-C PRS and LDL-C was associated with a 1.20 (95% CI, 1.12–1.28) -fold and 1.12 (95% CI, 1.03–1.22) -fold increased odds of IHD, respectively. The LDL-C PRS remained strongly associated with IHD incidence (OR, 1.27 [95% CI, 1.16–1.40]) after adjusting for measured LDL-C and other traditional risk factors.

The above results suggest that across different ancestries, the LDL-C PRS and measured LDL-C levels consistently showed comparable associations with the risk of IHD.

DISCUSSION

The present study reports a highly predictive LDL-C PRS, which explained an important degree of variation in LDL-C level among FH variant carriers, helping to explain the variable penetrance of FH variants. Among individuals with severe hypercholesterolemia, those with a low LDL-C PRS had a 21-fold higher probability of carrying an FH variant compared with those with a high LDL-C PRS. The LDL-C PRS showed a comparable association with IHD risk as measured LDL-C level. Last, the association between the LDL-C PRS and IHD was partly independent of LDL-C and other traditional IHD risk factors, suggesting that the LDL-C PRS may capture the lifelong exposure to heritable IHD risk through pleiotropic pathways.

The LDL-C PRS developed in this study explained 21% of the variance in LDL-C level in White British population in UK Biobank. Several PRSs were developed for LDL-C previously, of which the variance explained ranged from 3% to 18%.[9,15,16] Natarajan et al[10] generated a PRS for LDL-C consisting of over 2 million single-nucleotide

Table 5. Association Between LDL-C PRS and Other IHD Risk Factors

Risk factor	Correlation (95% CI)	Odds ratio* (95% CI)
Age	−0.00 (−0.01 to 0.01)	
Sex		0.99 (0.97 to 1.01)
Systolic blood pressure	0.01 (−0.00 to 0.02)	
Body mass index	0.00 (−0.01 to 0.01)	
Type 2 diabetes		1.02 (0.97 to 1.07)
Smoking (current)		0.97 (0.93 to 1.00)
Smoking (ever)		0.99 (0.97 to 1.01)
Triglycerides†	0.11 (0.10 to 0.12)	
Total cholesterol†	0.41 (0.41 to 0.42)	
HDL-C†	−0.05 (−0.06 to −0.04)	
Lipoprotein (a)	0.11 (0.01 to 0.12)	
Apolipoprotein B†	0.48 (0.48 to 0.49)	

HDL-C indicates high-density lipoprotein cholesterol; IHD, ischemic heart disease; LDL-C, low-density lipoprotein cholesterol; and PRS, polygenic risk score.

*Odds ratios were calculated per SD increase in the LDL-C PRS.

†Triglycerides, total cholesterol, HDL-C, and apolipoprotein B levels have been adjusted according to individual's medication status.

polymorphisms using LDpred,[17] which explained 29% of the variance in LDL-C in the training set. The variance explained in their test set was not reported and may be closer to what we observed in our study. This improvement in the variance explained in LDL-C may enable a more precise evaluation of the potential clinical implications of the LDL-C PRS.

Previous studies demonstrating the additional CVD risk imposed by pathogenic FH variants supported the possible need for routine genetic testing of FH among individuals with suspected symptoms, such as severe hypercholesterolemia.[4,12,18,19] In clinical practice, the identification of FH carriers has important consequences for reimbursement of therapies such as PCSK9 (Proprotein Convertase Subtilisin/Kexin Type 9) inhibitors to prevent potential CVD outcomes. However, the wide adoption of genetic testing of FH among hypercholesterolemia patients is still hindered by its high cost and other administrative barriers.[20] By using a relatively inexpensive genome-wide genotyping profile to generate an LDL-C PRS, we have shown that triaging by the PRS may help increase the yield of genetic testing by increasing the probability of identifying FH patients.[20–23]

We note that the enrichment of FH variant carriers among severe hypercholesterolemia patients with a low LDL-C PRS was likely to be a result of collider bias.[13] The rare FH pathogenic variants and polygenic predisposition are independent causes of severe hypercholesterolemia which becomes a collider. Sample selection or statistical analysis conditioning on the collider (severe hypercholesterolemia) will then lead to an association between the 2 causes, the extent of which depends on the strengths of the causal relationships between the genetic causes and the common outcome. Such association between independent causes cannot otherwise be

observed in the general population without conditioning on the collider. Our finding showed that the mechanism of collider bias may be useful to tailor rare variant screening for FH by using an LDL-C PRS.

The LDL-C PRS was associated with IHD risk to a similar magnitude as measured LDL-C level, and such association was partly independent of LDL-C and other IHD risk factors. This indicates that genetically predicted LDL-C may estimate the cumulative lifelong exposure to elevated LDL-C of an individual. Therefore, the findings support the possible use of PRS in CVD risk evaluation, especially in early life, to inform lifestyle and pharmacological interventions.

Our study, of course, has important limitations. First, the findings were not validated in an independent cohort. As such, the clinical relevance of the findings remains to be replicated. Second, disease risk models should be calibrated before clinical use. Here, we have used WES to identify FH carriers in a research context. Using clinical-grade sequencing may serve to identify different individuals harboring variants, particularly at lower minor allele frequencies that impact LDL-C levels. We have defined a clinically relevant outcome IHD, rather than coronary artery disease which might be of interest. Using this definition of IHD has permitted inclusion of individuals with clinical symptoms, such as angina pectoris, which is often reported as an outcome in cardiovascular prevention trials.[24,25] Only incident cases of IHD occurring after the LDL-C were used to test the association between LDL-C and IHD, but the exposure to similar levels of LDL-C could have initiated before the measurement. The association between LDL-C and IHD might thus have been underestimated. Yet, this provides evidence for the fact that a single LDL-C measurement does not accurately represent the cumulative lifelong exposure to LDL-C of an individual and genetically predicted LDL-C could be helpful. The association between the LDL-C PRS and risk of IHD was not conclusive among FH variant carriers, likely due to the reduced statistical power in the small sample size. Furthermore, the LDL-C PRS was developed in UK Biobank White British participants aged between 39 and 73 years old at baseline, who are generally healthier than the general population. The developed PRS was further validated in UK Biobank non-White British European and South Asian participants, respectively. Although the associations with the clinical outcomes remained consistent, a decrease in the predictive performance of PRS was observed. This suggests that the transferability of the PRS in other populations, particularly those of difference ancestry, remains to be addressed. Last, we note that the LDL-C PRS may include FH-associated variants of which the pathogenicity is not yet clear, and some single-nucleotide polymorphisms in the PRS might be in linkage disequilibrium with FH variants. However, little difference in the association between LDL-C PRS and LDL-C or IHD was observed when adding FH variant status as a covariate.

CONCLUSIONS

An LDL-C PRS may help identify individuals at higher risk of FH and IHD, thus helping to target testing, screening, and intervention in the clinical setting.

ARTICLE INFORMATION

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Disclosures

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