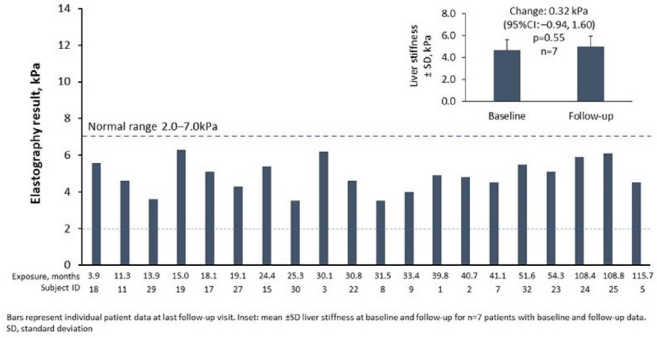
all patients (Figure) and the mean FIB-4 score remained below the fibrosis threshold value of 2.67.
Conclusions: Overall, the hepatic safety of lomitapide remains favourable with no clinically significant elevations in hepatic biomarkers and hepatic elasticity remained normal for up to 9.5 years in patients with HoFH.



Bars represent individual patient data at last follow-up visit. Inset: mean ±SD liver stiffness at baseline and follow-up for n=7 patients with baseline and follow-up data. SD, standard deviation

Figure. Hepatic elasticity in lomitapide-treated HoFH patients with follow-up elastography (n=20).

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Oral 03

Prevalence of familial hypercholesterolaemia (FH)-causing variants and impact on LDL-C concentration in European, South Asian, and African ancestry groups of the UK Biobank

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Background: Familial Hypercholesterolaemia (FH) is a genetic disease of high low-density lipoprotein cholesterol (LDL-C) with higher risk of premature cardiovascular disease. The prevalence of FH-causing variants and their association with LDL-C in non-European populations remains largely unknown. Using DNA diagnosis of FH in a population-based cohort we aimed to estimate the frequency of FH variants across three major ancestry groups in the UK.
Material and Methods: Principal component analysis (PCA) was used to distinguish genetic ancestry in UK Biobank participants. Whole exome sequencing (WES) data were analysed to provide a genetic diagnosis of FH. LDL-C concentrations were adjusted for statin use.
Results: PCA distinguished 140,439 European (Eur), 4,067 South Asian (SA), and 3,906 African (Afr) participants with lipid and WES data. There were significant differences between the three groups, including total cholesterol and LDL-C concentrations, as well as prevalence and incidence of coronary heart disease. We identified 488 Eur, 18 SA, and 15 Afr participants with a likely pathogenic or pathogenic variant for FH. No statistical difference in the prevalence of an FH-causing variant was observed: 1/288 (95%CI: 1/316;1/264) in Eur, 1/260 (95%CI: 1/526;1/173) in Afr, and 1/226 (95% CI: 1/419;1/155) in SA. Carriers of an FH-causing variant had significantly higher LDL-C concentration than non-carriers, in every ancestry groups. However, there was no difference in mean (statin-use adjusted) LDL-C concentration in FH-variant carriers depending on their ancestry background. Self-reported statin use was highest in FH-variants carriers of SA ancestry (55.6%), followed by Afr (40%) and Eur (33.8%), but it wasn't statistically significant.
Conclusions: The prevalence of FH-causing variants in the UK Biobank is similar across the ancestry groups analysed. Despite overall differences in lipid concentrations, FH-variant carriers across the three ancestry groups had similar LDL-C, and the commonly used FH diagnostic threshold of LDL-C >4.9 mmol/L performs similarly at detecting affected Eur, SA and Afr FH individuals. In all ancestry groups, the proportion of FH-variant carriers treated with lipid-lowering therapy should be improved to reduce future risk of premature cardiovascular disease.

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Oral 04

How many individuals with Familial Hypercholesterolaemia (FH) need to be identified to achieve the NHS 2019 Long Term Plan ambition?

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Background: The NHS 2019 Long Term Plan (LTP) set an ambition of identifying 25% of the predicted FH patients in England. The best current estimate of the number of genetically identified FH individuals is ~9000, which is ~4% of the predicted total. Here we use published and unpublished data to estimate the UK prevalence of individuals carrying an FH-causing variant.
Methods: A literature search was used to identify published papers and pre-prints with Next Generation Sequencing data covering the *LDLR/APOB/PCSK9* genes, known to harbour the majority of FH-causing variants, obtained from population-based UK subjects.
Results: The table below includes data from four population-based samples of UK (white British) adults and children.

Study	Description (mean age)	Number sequenced	Number FH-Variant	Prevalence (95%CI)	Reference
UK 10K project	Non-FH adult index cases	1805	7	1:258 (1:128-1:991)	Walter et al 2015 PMID:26367797
Wald	Random UK sample at GP immunisation (12 months)	10095	37	1:273 (1:198-1: 388)	Wald et al 2016PMID:27783906
ALSPAC	Healthy Bristol children (9 yrs)	1512	6	1:252 (1:140-1:1249)	Futema et al 2017PMID:28349888
UK BioBank	Healthy UK (white) adults (55 yrs)	140,439	488	1:288 (1:263-1:315)	Gratton et al in press*
Overall		**153,851**	**538**	**1:286 (1:263-1:311)**	

*https://www.medrxiv.org/content/10.1101/2022.06.17.22276540v1

Point estimates range from 1:252 to 1:288. Infants and children should provide the least biased estimate since there should be no loss of FH-causing alleles because of death from early CHD. There was some evidence that the prevalence was marginally higher in the child/infant cohorts than the adult BioBank cohort, but the confidence intervals (CI) overlap and these differences were not statistically significant. Combining the data gives an overall prevalence estimate of 1:286 with 95% CI of 1:263-1:311.
Conclusions: Based on the population size of England in 2022 of 56.5million this prevalence gives an estimate (95%CI) of 199,000 (183,000-216,000) individuals in the UK. The NHS LTP ambition of identifying 25% of the predicted number of FH individuals therefore requires the identification of 49,750 (51,240-54,000) individuals. With an estimated 9000 genetically confirmed FH patients known in England, this prevalence figure equates to an additional 40,750 individuals to be identified.

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