Family history of premature cardiovascular disease: blood pressure control and long-term mortality outcomes in hypertensive patients

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Aims
Current guidelines recommend early referral and initiation of intensive cardiovascular (CV) risk reduction in individuals with a positive family history of coronary heart disease (CHD). We hypothesized that a family history of premature CHD and stroke [CV disease (CVD)] would lead to earlier referral of hypertensive patients to secondary care clinic, leading to better control of risk factors, mitigating the excess risk seen in these individuals.

Methods and results
We studied the association of a positive family history of CVD in 10 787 individuals with longitudinal changes in risk factors and long-term cause-specific mortality in the Glasgow Blood Pressure Clinic using generalized estimating equations and the Cox proportional hazard models, respectively. The total time at risk was 193 756 person-years with a median survival time of 29.2 years. A positive family history of CVD was associated with an earlier presentation to the clinic, a lower burden of traditional CV risk factors, and similar longitudinal blood pressure reduction and drug adherence compared with those without. But despite these positive features, all-cause [hazard ratio (HR) = 1.12, 95% confidence interval 1.01–1.25] and CV (HR = 1.20, 1.04–1.38) mortality independent of baseline risk factors were worse. Consistent results were observed in propensity score-matched analysis. Inclusion of family history of CVD did not improve mortality risk discrimination over and above traditional risk factors.

Conclusion
Our study suggests that despite earlier referral and treatment of individuals with a positive family history of premature CVD, excess risk persists, indicating the need for continued and sustained efforts to reduce risk factors and drug adherence in these individuals.

Keywords
Hypertension • Family history • Mortality • Epidemiology

Introduction
Familial aggregation of coronary heart disease (CHD) is well recognized, and a family history of premature CHD has been consistently reported to be an independent risk factor for CHD.¹–⁷ This has been incorporated in many commonly used cardiovascular (CV) risk prediction scores⁸–¹¹ but not Framingham risk score.¹² While most evidence come from short-term risk studies, the risk due to parental history of premature vascular disease has also been shown to be associated with a greater lifetime risk of CHD mortality in a large cohort with lower risk factor burden and higher socioeconomic status.¹³ As the scientific evidence for CV disease (CVD) prevention is compelling,¹⁴ a positive family history should result in a greater awareness of risk leading to personal and physician-initiated attempts to make favourable changes in lifestyle and possibly earlier intensive risk factor modification measures. However, the extent to which these measures lead to abrogation of the increased risk is unclear. Numerous genetic and...
non-genetic factors are responsible for the familial aggregation of CVD, and the magnitude of contribution of these factors may have an impact on the attenuation of risk after known modifiable traditional risk factors are controlled.

We hypothesized that a family history of premature CVD would lead to earlier referral of hypertensive patients to a specialist secondary care clinic, leading to better control of risk factors, mitigating the excess risk seen in these individuals. We examined the association between family history of premature CVD and long-term mortality in a large treated hypertensive cohort with 35-year follow-up for mortality.

Methods

Study setting and study population

Glasgow is the largest city in Scotland with a population of 2.3 million representing 41% of Scotland’s population. The Greater Glasgow area is a contiguous urban area within the city of Glasgow with a population of 1.2 million. The Glasgow Blood Pressure Clinic (GBPC) located in the Greater Glasgow area is the largest and the main specialist hypertension clinic in Glasgow and provides secondary and tertiary level service to patients with hypertension in Glasgow. Patients are referred to the GBPC if their blood pressures (BPs) are not controlled in primary care with at least three drugs or if there is evidence of high-risk factors such as early-onset hypertension, features of secondary hypertension, or family history or premature CVD. Structured instruments are used to collect data from all patients attending the clinic and are stored electronically in a single computerized database, which contains information on 16 011 patients attending the clinic from 1969 until 2011. The West of Scotland research ethics service (WoSRES) of the National Health Service has approved the study of the GBPC database (11/WS/0083).

Clinical measurements

The GBPC employs specialist hypertension nurses who are experienced and highly trained in BP measurement.15 The procedure required subjects to rest for 5 min in a seated position before BP was manually measured using standard sphygmomanometers and Korotkoff sounds (phase V) were used for estimating diastolic BP (DBP). Three BP measurements were performed, 1 min apart, and the mean of the second and third measurements was recorded. Patients attending the clinic were advised to take their regular medications as usual. Each patient attended the same clinic; therefore at each visit, their BP measurement would occur in the same 3 h time window either in the morning or afternoon. Height and weight of all patients were measured using standardized equipment during each visit in order to calculate body mass index (BMI). Blood samples were collected at baseline and at regular intervals for estimation of routine haematological and biochemical indices. All biochemical investigations were performed at the Western Infirmary clinical laboratory service. Glomerular filtration rate (GFR) was estimated using modification of diet in renal disease equation. Both tobacco (any vs. none) and alcohol use (quantity and frequency of consumption) were assessed using a structured format during the clinic visit.

Family history assessment

Records of patients who attended the GBPC from 1969 to 2011 were extracted from the database and reviewed. Each patient attending the clinic completed a structured questionnaire on health details of first-degree relatives (parents and siblings): alive/dead, number of full brothers and full sisters, history of hypertension, myocardial infarction and stroke, age at death, age at heart attack/stroke, and age at diagnosis of hypertension. The cause of death for each parent or sibling was recorded as free text and this was manually classified into eight categories—respiratory, possible respiratory, CV, possible CV, cancer, possible cancer, other, and not known. Family history of CVD was determined using the ASSIGN criteria for premature vascular disease—development of heart disease or stroke before the age of 60 years in parent or sibling. We divided patients into four groups based on their history of premature CVD in their parents or first-degree relatives: P-FH and P-FH were, respectively, groups with or without a parental history (either or both parents) of premature CVD. FDR-FH and FDR-FH were groups with or without a first-degree relative with premature CVD.

Outcome assessment

Records kept by the General Register Office for Scotland ensured notification of a subject’s death (provided that it occurred in the UK) together with the primary cause of death according to the International Classification of Diseases, 10th Revision, Version for 2007 (ICD-10), codes. We considered CV deaths (CV mortality; ICD-10 codes I00-I99), ischaemic heart disease deaths (IHD mortality; ICD-10 codes 120-I25), and stroke deaths (stroke mortality; ICD-10 codes 160-169) in the analysis. Deaths not due to these conditions were classified as non-CV deaths. Mortality data were collected up to April 2011.

Adherence assessment

Data on refilled prescriptions were available on a subset of patients through the Information Services Division (ISD) for NHS Scotland. The Prescribing Information System holds information on 100% of NHS Scotland prescriptions dispensed within the community and claimed for payment by a pharmacy contractor (i.e. pharmacy, dispensing doctor, or appliance supplier). It does not include data on prescriptions dispensed but not claimed (likely to be very small) or prescriptions prescribed but not submitted for dispensing by a patient. Prescription data were available from 2004 onwards on alive subjects. Although the subgroup in whom prescription data were available may not be representative, we selected a group in whom we had prescription data for at least 5 years to assess differences in adherence to CV drugs based on family history. We calculated the average annual refill rate of antihypertensive, antplatelet, and lipid-lowering drugs for each patient during this period of review as measures of adherence. This does not account for drugs dispensed to the patient but subsequently not taken by the patient in accordance with dosage instructions.

Statistical analysis

Differences in baseline characteristics in groups with and without positive family history of CVD were explored using independent t-test (for continuous variables) and χ² test (for categorical variables).

We explored the effect of positive family history on longitudinal changes in BP, cholesterol, BMI, and estimated GFR (eGFR) using generalized estimating equations (GEE). Individuals with at least four annual measurements in the first 5 years of follow-up, a 5-year minimum follow-up period, and survival up to a minimum of 5 years were included in this analysis. The association was adjusted for conventional covariates—baseline age, sex, alcohol and tobacco use, BMI, cholesterol, and eGFR as appropriate. All non-missing pairs of data were used in estimating the working correlation parameters.

The Cox proportional hazard (Cox-PH) models were used to analyse the relationship between a positive family history of CVD on all-cause, CV, IHD, stroke, and non-CV mortality. We present the unadjusted (Model 1) and adjusted results separately (Models 2–4). A variable on year of first visit strata (epochs) was used to adjust the secular trend in mortality (Model 2) and was divided into five categories (first visit 1977
or before, between years 1978–85, 1986–93, 1994–2001, 2002 and thereafter). Model 3 is adjusted for baseline age, sex, and epochs. Model 4 was adjusted for baseline age, gender, epochs, BMI, smoking status (never vs. ever), systolic BP (SBP), alcohol use, baseline prevalence of CVD, and chronic kidney disease (CKD) status (eGFR < 60, eGFR ≥ 60). The proportional hazards assumption was verified through examination of log-minus-log plots.

Propensity score matching (nearest neighbour) was used to match patients with and without a positive family history of CVD. Cox-PH models were generated in the matched population to study the independent association of family history of CVD and different types of mortality outcomes.

The discriminatory power of positive family history of CVD in predicting CV mortality was assessed using ‘C-statistics’, net-reclassification improvement, and integrated discrimination improvement.16,17 Stata version 12.0 (Statacorp) was used for all statistical analysis.

Results

Demographic and clinical characteristics of the study population

Baseline characteristics are shown in Table 1 for the overall population and in Supplementary material online. Table S1 for the propensity score-matched group. There were 1408 and 9379 individuals, respectively, with (P-FH+) and without parental history (P-FH) of premature CVD, while 1864 individuals (FDR-FH+) had at least one first-degree relative with premature CVD and 7571 individuals (FDR-FH) had no first-degree relative (both parents negative) with premature CVD. More than half (51.7%) of the study participants were female, the mean BMI was 27.1 ± 5.2 kg/m², the mean baseline SBP was 169.6 ± 29.6 mmHg, the mean baseline DBP was 100.1 ± 15.3 mmHg, and 23% had at least stage 3 CKD. At first clinic visit, compared with P-FH+, P-FH were younger, had lower BP, lower cholesterol, and less prevalent CKD. As the ascertainment period was very long, the baseline demographic profile of patients presenting in different time-periods (epochs) is presented in Figure 1 showing no substantial between-group differences across epochs. The total time at risk was 193,756 person-years with a median survival time of 29.2 years. The incidence rates were 20.5 (95% confidence interval (CI) 19.9–21.1), 13.8 (95% CI 13.3–14.3), and 8.9 (95% CI 8.5–9.4) per 1000 person-years of follow-up for all-cause, CVD, and non-CVD mortality, respectively.

Association between family history of CVD and mortality

Unadjusted and adjusted results of Cox survival analyses are presented in Table 2. In the univariate analysis, P-FH+ was associated with lower mortality (Model 1), but this was reversed after inclusion of age, without any major attenuation of hazard ratios between models adjusted for age and sex (Model 3) and the fully adjusted model (Model 4). In the fully adjusted model, FDR-FH+ and P-FH+ were associated with an 11–12 and 14–20% increased risk of all-cause and CV death, respectively. There was no association with non-CV or stroke mortality. The results were similar in the propensity-matched analysis.

Association of family history of cardiovascular disease with longitudinal blood pressure and estimated glomerular filtration rate

In the GEE analyses, the overall average annual reduction in SBP in the first 5 years was −3.4 (SE 0.06) mmHg and DBP −1.9 (0.03) mmHg after adjustment for age, sex, BMI, smoking, alcohol use, CKD, and prevalent CVD. Family history had no effect on 5-year changes in BP, eGFR, or cholesterol (Figure 2 and Supplementary material online, Table S2).

Discriminatory power of family history of cardiovascular disease in predicting cardiovascular mortality

Reclassification analyses (Table 3) showed that the inclusion of family history of CVD did not improve CV mortality risk.

Table 1 Baseline characteristics of the study population

<table>
<thead>
<tr>
<th>Variables</th>
<th>Parental FH</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>50.30 (13.59)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Women, n (%)</td>
<td>4821 (51.40)</td>
<td>0.088</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.97 (5.10)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>170.34 (29.75)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>100.17 (15.41)</td>
<td>0.008</td>
</tr>
<tr>
<td>Total cholesterol (mmol/L)</td>
<td>6.13 (1.27)</td>
<td>0.054</td>
</tr>
<tr>
<td>Haematocrit (%)</td>
<td>0.43 (0.04)</td>
<td>0.883</td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td>4386 (47.14)</td>
<td>0.514</td>
</tr>
<tr>
<td>Alcohol &gt;6 units per week, n (%)</td>
<td>5940 (64.64)</td>
<td>0.727</td>
</tr>
<tr>
<td>CKD, n (%)</td>
<td>1966 (22.41)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CVD, n (%)</td>
<td>1705 (18.18)</td>
<td>0.302</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>FH in first-degree relatives</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>50.01 (13.80)</td>
</tr>
<tr>
<td>Women, n (%)</td>
<td>3873 (51.16)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.50 (5.60)</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>169.98 (28.94)</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>100.13 (15.43)</td>
</tr>
<tr>
<td>Total cholesterol (mmol/L)</td>
<td>6.11 (1.27)</td>
</tr>
<tr>
<td>Haematocrit (%)</td>
<td>0.43 (0.04)</td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td>3545 (47.15)</td>
</tr>
<tr>
<td>Alcohol &gt;6 units per week, n (%)</td>
<td>4791 (64.26)</td>
</tr>
<tr>
<td>CKD, n (%)</td>
<td>1561 (22.38)</td>
</tr>
<tr>
<td>CVD, n (%)</td>
<td>1321 (17.45)</td>
</tr>
</tbody>
</table>

Data presented as mean ± SD unless otherwise specified. FH, family history; CVD, cardiovascular disease; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; CKD, chronic kidney disease.
discrimination over and above conventional CV risk factors, but reclassification improved by 1.9% using risk cut-offs of 0–10%, 10–20%, and >20%.

**Drug adherence**
Dispensed prescription data were available on 1869 patients for at least 5 years between 2004 and 2013 with 5.8 ± 2.9 years interval...
between their first clinic visit and the start of the prescription review period. FDR-FH+ and P-FH+ were younger than those with no family history. All patients were on antihypertensive treatment during this period, the average refill rate was 5.8 ± 1.9, and 51% of patients had a coefficient of variation <1 of the inter-refill interval. There was no significant difference in the annual rate of refilled prescriptions or coefficient of variation of inter-refill interval based on parental or family history of CVD (Table 4).

Discussion

In this study of a large cohort of treated hypertensive patients with long follow-up, P-FH+ was associated with an earlier presentation to the clinic, a lower burden of traditional CV risk factors, and similar longitudinal BP reduction compared with P-FH+. However, this did not translate into improved long-term CV outcomes, rather we show despite active management of CV risk factors in a tertiary care centre, P-FH+ had a higher 35-year CV mortality compared with those without. The results were consistent in both FDR-FH+ and in the propensity score-matched analyses. A positive parental history of CVD failed to substantially improve the discriminatory power of the risk models over and above traditional risk factors, but there was a slight improvement in risk reclassification.

P-FH+ individuals presented earlier to clinic, and this may be due to greater awareness, shorter referral time, or earlier onset of hypertension. However, P-FH+ also had lower BP at presentation along with lower cholesterol and less renal disease, indicating better awareness of future CV risk as a probable reason for referral. In a subset of patients in whom accurate data on prescription refill were available for at least 5 years, similar patterns of drug adherence were observed for antihypertensive, lipid-lowering, or antiplatelet drugs. Moreover, only 48–50% of subjects were taking antiplatelet drugs. There is evidence that awareness of a family history of CVD can result in positive

Table 3 Prediction of cardiovascular mortality

<table>
<thead>
<tr>
<th>Predictive models</th>
<th>C-statistics</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline model</td>
<td>0.799</td>
<td>0.778–0.810</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Baseline + Parental FH</td>
<td>0.801</td>
<td>0.792–0.819</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Baseline model</td>
<td>0.793</td>
<td>0.779–0.807</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Baseline + FH FDR</td>
<td>0.795</td>
<td>0.775–0.809</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Coefficient</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>NRI (FH FDR)</td>
<td>0.019</td>
</tr>
<tr>
<td>IDI (FH FDR)</td>
<td>0.056</td>
</tr>
</tbody>
</table>

FH, family history; FDR, first-degree relatives; CI, confidence interval; NRI, net reclassification improvement; IDI, integrated discrimination improvement. Adjusted for age, sex, body mass index, smoking, alcohol use, systolic blood pressure, cholesterol, chronic kidney disease status, and baseline cardiovascular disease.
changes in behavioural and lifestyle.\textsuperscript{2,18} It is to be expected that earlier adoption of healthier lifestyle and early risk factor intervention should lead to significant mitigation of risk over the long term.\textsuperscript{19} While our results are surprising, it needs to be interpreted taking into consideration all the positive features observed—early referral and no difference in longitudinal reduction in BP, which may have partially mitigated the excess risk. In our population, we do not have data to assess what the true risk would have been, had individuals with positive family history not been referred to the clinic. Moreover, while competing risks may have influenced our results for 35-year mortality risk, we show that CV mortality is still significantly higher over the long follow-up period. Interestingly, the Cooper Center Longitudinal Study\textsuperscript{13} showed findings similar to ours, albeit in a low-risk population cohort, where the presence of positive family history of premature vascular disease was associated with a 5% absolute and 50% relative difference in the lifetime risk for CVD and CVD mortality, and this risk was consistent across the short term (< 10 years) and long term (> 20 years) of follow-up. Taken together, the implication is that the presence of family history of premature CVD represents a clinically significant sustained increase in CHD and CVD risk across the lifespan, and the pathological processes determining this increased risk must start long before the traditional risk factors are identified and treated. Also, current risk reduction strategies may need to be optimized to minimize the excess lifetime risk posed by a positive family history.

There is unequivocal evidence that even relatively low burden of traditional risk factors translates into markedly higher lifetime risks of CVD across the lifespan.\textsuperscript{19} To our knowledge, we are the first to show that current primary prevention strategies do not completely abolish the excess risk from a positive parental history. There are three possible explanations for our findings. A positive family history may reflect (i) genetic factors that affect known risk factors like PSCK9 non-sense mutation,\textsuperscript{20} which can result in sustained exposure from birth and hence significant cumulative lifetime CV risk; (ii) novel mechanisms unrelated to traditional risk factors—if this is the case, there would be evidence of considerable improvement in discrimination and re-classification of short-term risk. But this is not observed in either our study or the Framingham and EPIC-Norfolk studies;\textsuperscript{3,4} (iii) onset of sustained damage to the vascular system much earlier than presentation—epidemiological evidence supporting this include the presence of significant subclinical atherosclerosis in one-third of asymptomatic women with a sibling history of early-onset CVD;\textsuperscript{21} children of hypertensive parents show a more rapid rise in BP, higher arterial stiffness, and greater left ventricular mass than those of normotensive parents.\textsuperscript{22–25} It is likely that family history can reflect a combination of these factors resulting in early vascular injury that is not effectively reversed with later interventions.

The strengths of the current study include the large cohort size, long follow-up, longitudinal clinic and laboratory measurements, and mortality outcomes. Our study has limitations which include its observational nature and the study subjects derived from a predominantly urban hypertension clinic. We have no data on diet or physical activity within our study. Although we had drug prescription data only from 2004, our metrics of drug adherence are reliable as the data are from at least 5 years of prescription refill data and more representative of current population. Almost all our subjects were Caucasians, so our results may not be applicable to other ancestries. Confounding may be an issue when assessing the relationship between family history and mortality outcomes. Although the GBPC is the only specialist hypertension clinic in the catchment area, patients with mild hypertension are usually not referred to the clinic. However, as the primary hypothesis is related to patients with premature CVD who are all referred to the clinic, this may not have a major impact, but a residual issue with differential selection cannot be completely excluded. Risk factor clustering occurs in families and sharing of higher levels of CV risk factors may lead to inflated risk estimates from a positive family history. In order to record a case as having a premature history of CVD in one of their siblings, families need to include a minimum of one proband. Larger families will be more likely to have a first-degree relative with a positive history, and therefore, it is possible that our analysis was disproportionately driven by an increased number of recorded events in larger families. Another type of bias we cannot exclude is survivorship bias. This refers to the possibility that individuals with more severe phenotypic disease expression may have died prior to clinic attendance. Patients included in our study

### Table 4: Adherence to cardiovascular medications in patients with dispensed prescription data for more than 5 years (2004–13)

<table>
<thead>
<tr>
<th></th>
<th>$Nin^a$</th>
<th>P-FH$^b$</th>
<th>P-FH$^+$</th>
<th>$P$-value</th>
<th>$Nin^b$</th>
<th>FDR-FH$^b$</th>
<th>FDR-FH$^+$</th>
<th>$P$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at the start of prescription review period (years)</td>
<td>1493/376</td>
<td>58.56 (12.63)</td>
<td>54.24 (11.14)</td>
<td>&lt;0.001</td>
<td>1303/566</td>
<td>58.07 (12.78)</td>
<td>56.81 (11.67)</td>
<td>0.04</td>
</tr>
<tr>
<td>Interval between first clinic visit and prescription review period (years)</td>
<td>1493/376</td>
<td>5.7 (2.9)</td>
<td>5.8 (3.0)</td>
<td>0.71</td>
<td>1303/566</td>
<td>5.8 (2.9)</td>
<td>5.8 (3.0)</td>
<td>0.69</td>
</tr>
<tr>
<td>Annual rate of refilled prescriptions</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antihypertensive</td>
<td>1488/374</td>
<td>5.83 (1.92)</td>
<td>5.76 (2.05)</td>
<td>0.49</td>
<td>1299/563</td>
<td>5.81 (1.93)</td>
<td>5.82 (2.01)</td>
<td>0.92</td>
</tr>
<tr>
<td>Antiplatelet</td>
<td>816/201</td>
<td>3.41 (2.23)</td>
<td>3.44 (2.37)</td>
<td>0.88</td>
<td>695/322</td>
<td>3.41 (2.24)</td>
<td>3.43 (2.28)</td>
<td>0.88</td>
</tr>
<tr>
<td>Lipid lowering</td>
<td>1014/256</td>
<td>3.95 (2.2)</td>
<td>3.83 (2.18)</td>
<td>0.44</td>
<td>861/409</td>
<td>3.92 (2.2)</td>
<td>3.93 (2.19)</td>
<td>0.94</td>
</tr>
</tbody>
</table>

Data presented as mean and standard deviation.

$^a$Number P-FH / number P-FH$^+$.

$^b$Number FDR-FH / number FDR-FH$^+$.
may therefore have had less severe disease which may have diluted the results of our study. Self-report data have the potential to introduce recall bias; however, studies have found these methods of data collection are reliable with respect to family history of CVD.36

Our study has important implications in clinical practice and underlines the importance of screening and prevention strategies to be adopted in primary and secondary care settings. Our finding that individuals with family history of premature CVD are referred earlier for primary prevention is encouraging; however, this may not be the case in general. There is evidence that despite higher prevalence of modifiable risk factors among relatives of probands with premature CVD and guideline recommendations, in practice they are not actively targeted for treatment.27–31 In a subgroup analysis, we observed similar rates of prescription of lipid-lowering and antiplatelet drugs and did not see an increase in drug adherence among those with a positive family history. This is potentially an aspect of clinical practice to be addressed, especially in terms of increasing take-up of antiplatelet and lipid-lowering therapy, and improving adherence to all CV medications in those with a strong family history of premature CVD. Current treatment guidelines are based on risk scores which interpret an individual’s risk using a population-based model which may not pick individuals in the lower- or medium-risk groups that account for the majority of CVD events. The identification of a CV risk factor or the occurrence of a CV event in an individual before the age of 60 should necessitate active intervention in their children, even if they do not manifest abnormal findings, to reduce future CV risk. Very few studies have evaluated the impact of interventions on family members of patients with CVD, and most of them focused on lifestyle interventions. But all these studies showed promising positive effects of the intervention on traditional risk factors among family members.31–34 Additionally, targeted dietary and exercise interventions need to be encouraged as there is evidence that the benefits of exercise on BP and outcomes may be intensity dependent.35 Smoking cessation is an important aspect of risk reduction measures and we find the presence of any family history of premature CVD had no impact on smoking status in our patients. Scotland’s tobacco control strategy is one of the most comprehensive in Europe and includes smoke-free legislation along with well-developed smoking cessation services and nicotine replacement therapy prescribing provided by the National Health Service. However, after the initial increase in smoking cessation attempts when smoke-free legislation was implemented, this has not been sustained, suggesting the need for additional tobacco control measures and ongoing support.37 Our study suggests that despite earlier referral and treatment of individuals with a positive family history of premature CVD, excess risk persists, indicating the need for continued and sustained efforts to reduce risk factors and drug adherence in these individuals. Additional prospective research is required to assess the utility and cost-effectiveness of primary prevention strategies in first-degree relatives of individuals with CVD or primordial prevention strategies for relatives of individuals who manifest a CV risk factor.

Supplementary material
Supplementary material is available at European Heart Journal online.

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Conflict of interest: none declared.

References


