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FULL RESEARCH PAPER
CVD risk factors

Influence of repeated plaque visualization on cardiovascular risk reduction after 3 years: a randomized controlled trial

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Aims Helping people to understand their cardiovascular (CV) risk can influence the choices they make for risk reduction, including medication adherence and lifestyle modification. This study sought whether repeated visualization of coronary artery calcium (CAC) images was effective in sustaining long-term risk control in primary prevention, independent of a risk reduction programme.

Methods and results Asymptomatic, statin-naïve participants, 40–70 years, with a family history of premature coronary artery disease and a CAC score from 1–400 were randomized to a nurse-led CV risk reduction programme or standard care with bi-annual reviews. Only the intervention group (220 of 449 participants) visualized their CAC image (with repeat exposure in the first 3 months) and were initiated on statin therapy. The primary outcome was change in Framingham Risk Score (FRS) at 36 months, and the impact of CAC image recall on CV risk was assessed. The reduction in FRS (difference in differences (DID) −3.4% [95% CI: −4.4% to −2.4%], $P \leq 0.001$ and low density lipoprotein cholesterol −1.2 mmol/L [95% CI: −1.4 to −1.0], $P \leq 0.001$) over 36 months was greater in the intervention than the control group. Within the intervention group, sustained recall of CAC images at 24 months was associated with lower systolic blood pressure (DID −4.3 mmHg [95% CI: −7.7 to −0.9], $P = 0.01$) and waist circumference (DID −2.0 cm [95% CI: −3.9 to −0.1], $P = 0.03$) at 36 months compared to unsustained recall.

Conclusion A nurse-led programme, combining personalized patient visualization of CAC imaging with statin therapy, is beneficial for improving CV risk. Recalling the presentation of CAC images through repeated visual exposure may influence risk reduction.

Registration Australia New Zealand Clinical Trials Registry: ACTRN12614001294640

Lay summary

- This trial sought to determine whether visualization of coronary artery calcium (CAC) images influences behaviour change and cardiovascular risk reduction within a structured nurse-led programme vs. standard care. Intervention participants visualized their personalized CAC images within the first three months and commenced statin therapy. Control participants were blinded to their CAC images and were not provided statin therapy.
- Intervention participants had a greater absolute reduction in the Framingham Risk Score (difference in differences −3.4% [95% CI: −4.4% to −2.4%], $P \leq 0.001$) compared to controls.
- Those with sustained recollection of their CAC images within the intervention group also had greater reductions in systolic blood pressure and waist circumference.

Keywords Cardiovascular risk • Coronary artery calcium • Framingham Risk Score • Nurse-led programme • Visualization

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Introduction

Cardiovascular disease (CVD) continues to be the foremost contributor to both mortality and morbidity on a global scale.[1] It is projected that, by the year 2030, CVD will account for more than 23 million global deaths.[2] The European Heart Network has estimated that CVD imposes an annual economic burden of over €200 billion on the European Union.[3] A key contributing factor to the increasing economic and disease burden of CV disease worldwide is the suboptimal implementation of primary prevention cardiovascular guidelines and poor adherence by individuals to primary prevention strategies.[3,4] Indeed, poor adherence is a widespread issue and is linked to increased risks of adverse health outcomes and mortality rates.[5,6] A recent review emphasized that nurse-led primary prevention programmes have the ability to overcome the challenges associated with poor adherence to CV risk factor modification.[7] Nurse-led programmes may enhance communication of CV risk and facilitate risk modification through patient-centred approaches and clinician prescribed tailored interventions.

The clinician–patient risk discussion forms the foundation for shared decision-making regarding the implementation of primary prevention strategies.[8] However traditional CV risk scores have been reported as being misunderstood or misperceived by asymptomatic individuals[9] resulting in suboptimal adherence to primary prevention strategies (statin therapy and lifestyle modification).[5,9,10] Incorporating CV imaging as a visual aid within the clinician–patient risk discussion may be a simple and feasible approach to engage with those at intermediate risk.[11–13]

The CAUGHT-CAD trial[14] seeks to demonstrate that coronary artery calcium (CAC)-guided management is associated with greater reduction of coronary plaque volume at 36 months than management without CAC guidance in 449 participants with a family history of premature coronary artery disease.[14] The identification of CAC serves as a reliable surrogate indicator of atherosclerosis and stands as a robust predictor for adverse CV events. Assessing CAC is readily accessible in primary care settings and has been integrated into the 2019 ACC/AHA Guideline on Primary Prevention of Cardiovascular Disease.[4] The CAUGHT-CAD intervention included patient visualization of CAC images to portray CV risk and the prescription of statin therapy, which resulted in lower Framingham Risk Score (FRS) over 12 months follow-up compared with usual care.[15] These findings align with a recent systematic review and meta-analysis that demonstrated an improvement of CV risk factors and reduction of predicted risk after patients visualized their CV images.[13,16] However, it remains unclear whether incorporating CAC image visualization into a nurse-led CV risk reduction programme could enhance an individual's adherence to preventative therapies and lifestyle management in the longer term. Accordingly, we hypothesized that the FRS would remain lower at 36 months in participants who visualized their personalized CAC image compared to those who did not visualize their CAC image. We also hypothesized that there would be a greater reduction in FRS and secondary outcomes at 36-month follow-up in those with sustained recollection of their personalized CAC images at 12 and 24 months compared to those with unsustained recollection in the control group.

Methods

Study design

This is a sub-study within the Coronary Artery calcium score: Use to Guide management of Hereditary Coronary Artery Disease (CAUGHT-CAD) trial (ACTRN 12614001294640). CAUGHT-CAD is an investigator-initiated, pragmatic, open-label, multi-centre, randomized controlled trial assessing the utility of CAC scoring for guiding risk evaluation and primary prevention statin therapy for individuals with a family history of early-onset coronary artery disease (*Figure 1*).

Details on criteria for eligibility and study design[14] and 12-month outcomes[15] have been previously published. The study protocol was approved by the Tasmanian Human Research Ethics Committee, University of Tasmania and conforms with the principles outlined in the Declaration of Helsinki. Written informed consent was obtained from all participants by a research nurse at the screening assessment visit.

Study population

Recruitment commenced October 2015 and ended in January 2019, across seven sites within Australia. A total of 1091 individuals from the community were screened for study eligibility. Inclusion was restricted to those aged 40 to 70 years, who had a family history of premature coronary artery disease defined as a first-degree relative < 60 years or second-degree < 50 years, no known history of any CV disease event, and were statin naïve at enrolment. Eligibility and screening criteria have been previously published[14] (*Figure 1*, Supplementary material online, *Tables S1* and *S2*).

Randomization

Randomization was done by the study co-ordinator at each site using a computerized protocol with a 1:1 ratio to the intervention or control group. Block-randomization was applied for the seven sites and randomization was stratified according to CAC score (>0 to 100 and 101 to 400).

Study intervention group

The intervention comprised a structured nurse-led CV risk discussion and patient visualization of their own personalized CAC images depicting subclinical coronary atherosclerosis along with their CAC score. The cardiac research nurse discussed the imaging results with the patient and provided individualized dietary, weight, smoking cessation, and physical activity goals to facilitate positive health outcomes. Reinforcement of CV risk modification with the use of personalized CAC images was repeated at visits with the cardiac research nurse, at 2 weeks, 4 weeks, and 3 months. From 6 months, the CAC image was used if requested by the participant during bi-annual visits. Atorvastatin 40 mg daily was assigned free of cost throughout the 36 months of follow-up. In the case of untreated hypertension, the cardiologist commenced anti-hypertensives as per current hypertension guidelines.[17] Primary care physicians were informed of their patients CAC score, classification of predicted CV risk, initiation of statin therapy by the study cardiologist and antihypertensive therapy where indicated.

Study control group

Standardized CV risk information informed by current CV prevention guidelines was provided by the cardiac research nurse focusing on modifiable risk factors including diet, exercise, and smoking cessation at baseline and at 6-month follow-up visits. However, the control participants and their primary care physicians were blinded to the CAC score and CT coronary angiogram images. Primary care physicians were informed that their patient had a calculated intermediate CV risk, identified subclinical coronary atherosclerosis and were participating in a 36-month study. These participants were able to attend to their general practitioner (GP) or seek other relevant concomitant care for treatment and ongoing follow-up.

Study procedures

Every participant was assessed at baseline and yearly visits at 12, 24, and 36 months to measure fasting lipid profile, blood pressure, waist measurement, smoking status, and pill counts for those on statin therapy. All participants received interim visits at 6, 18, and 30 months, including blood pressure, diet and exercise review, smoking status, and pill counts for those on statin therapy. Adherence to statin therapy was defined as taking 80% (292 tablets) or more of the yearly total.[18] Participants randomized to the intervention group and on statin therapy had liver function tests and were reviewed by the cardiac research nurse between 1 and 4 weeks post-randomization to evaluate statin tolerance. In the case of statin intolerance, a dose adjustment or an alternative statin was provided by the study cardiologist. All follow-up visits were completed in person or via telehealth during periods of lockdown due to the COVID-19 pandemic.

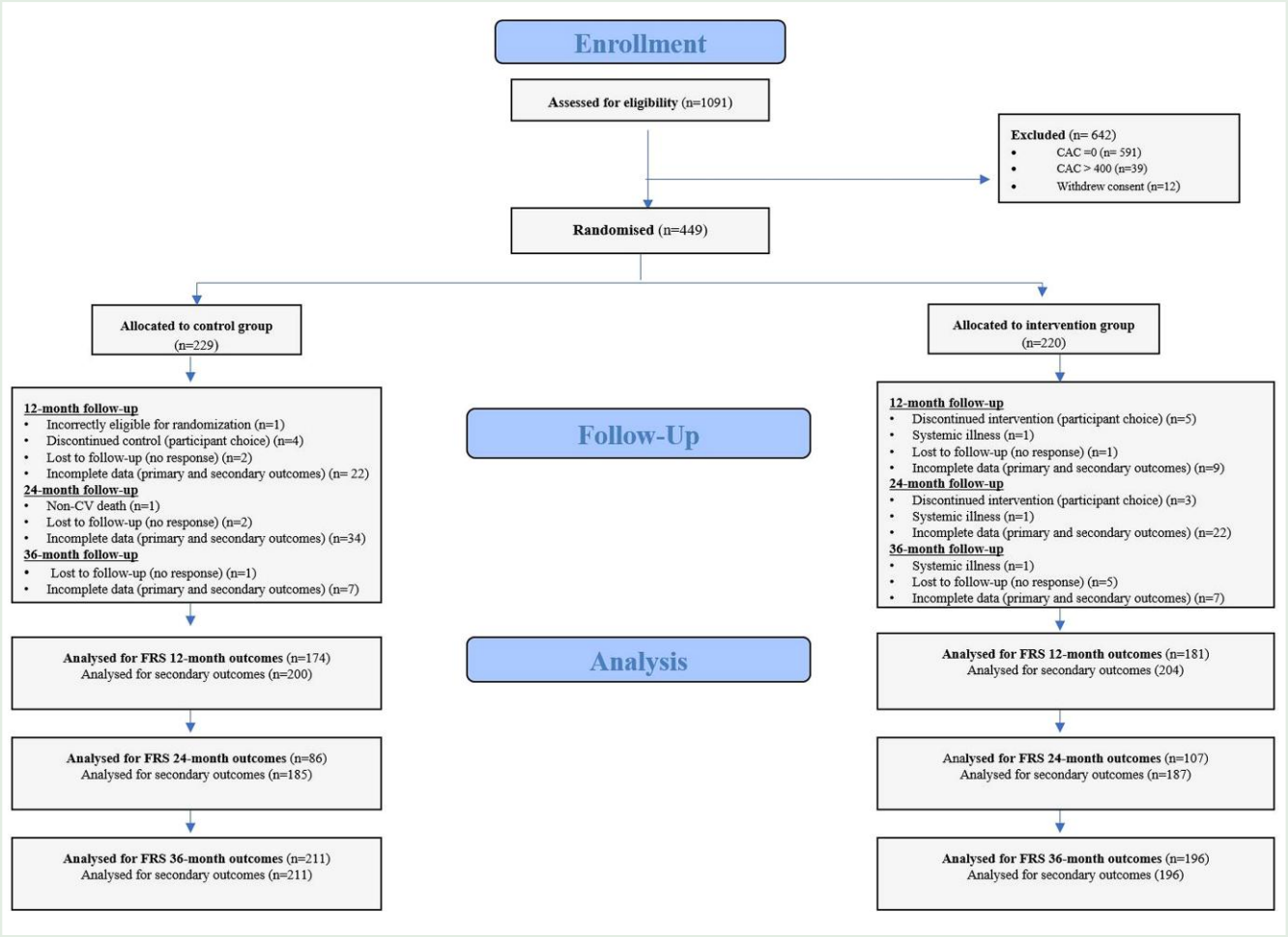

Figure 1 CONSORT diagram of the CAUGHT-CAD sub-study trial. Of the 449 individuals, 407 participants (91%) completed the 36-month follow-up. Those with early withdrawals over the 36 months in the control group ($n = 11$) and the intervention group ($n = 17$) were mainly due to participant choice and lost to follow-up (no response). The 36-month follow-up had a small percentage of missing data for the FRS (10%).

At 12- and 24-month follow-up visits, participants in the intervention group were asked a specific question at the beginning of the visit regarding recall of their recollection of their personalized CAC images: 'do you remember seeing the CAC image?' (*Figure 2*). Sustained recall was defined as self-reported recall of their CV image at 12- and 24-month visits, whereas unsustained recall was defined as not recalling their CAC image at either or both of 12- and 24-month visits. These responses were used to assess the influence of recall of CV images on changes in FRS and CV risk factors from baseline to 36-month follow-up.

Standardized measures of health status (EQ5D-5L), depression (PHQ9), and anxiety questionnaire (GAD) were completed by all participants at baseline and 36 months.

Study endpoints

The primary endpoint of this sub-study was the change in FRS (observed at one year in the CAUGHT-CAD study,[15]) from baseline to 36 months follow-up. Secondary endpoints were to assess change at yearly intervals in the primary outcome as well as individual CV disease risk factors including total cholesterol (TC), low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), blood pressure, body mass index (BMI), waist circumference (WC), smoking cessation, and adherence to primary prevention strategies (statin therapy, diet, and exercise). In addition, this study investigated the determinants of FRS change and the effect of sustained recall of CAC images on CV risk reduction in the intervention group (*Figure 2*).

Statistical analysis

All data were pooled and summarized with respect to demographic and baseline characteristics. The primary and secondary analyses were conducted according to intention-to-treat analyses. Baseline summary statistics are reported as mean with standard deviations or medians with interquartile ranges (IQRs) for continuous variables; categorical variables are summarized as numbers and proportions. We used multivariable linear regression model to estimate the difference in differences (DID) along with their 95% confidence intervals (CIs) between the control and intervention groups for primary and secondary outcomes from baseline to 12, 24, or 36 months. Adjustment was made for all baseline covariates that failed to reach balance between the randomized groups (diabetes) as well as age and sex in all analyses. Subgroup analyses were conducted for the absolute change in FRS by all baseline covariates. The primary analysis was also repeated for those in the intervention group comparing sustained vs. non-sustained CAC recall at both 12 and 24 months. A multivariable linear mixed effect regression model was used to compare the change in FRS and in other CV disease risk factors over time between the intervention and control groups. This model allows for missing data at 24 months due to COVID-19. The model was constructed by entering intervention group, follow-up visits (baseline, 6, 12, 18, 24, 30, 36 months), and their interaction and baseline covariates as fixed effect, and random intercept and slope as random effect.

All statistical tests were two-tailed and a P value of <0.05 was considered to indicate statistical significance. Analyses were performed using STATA

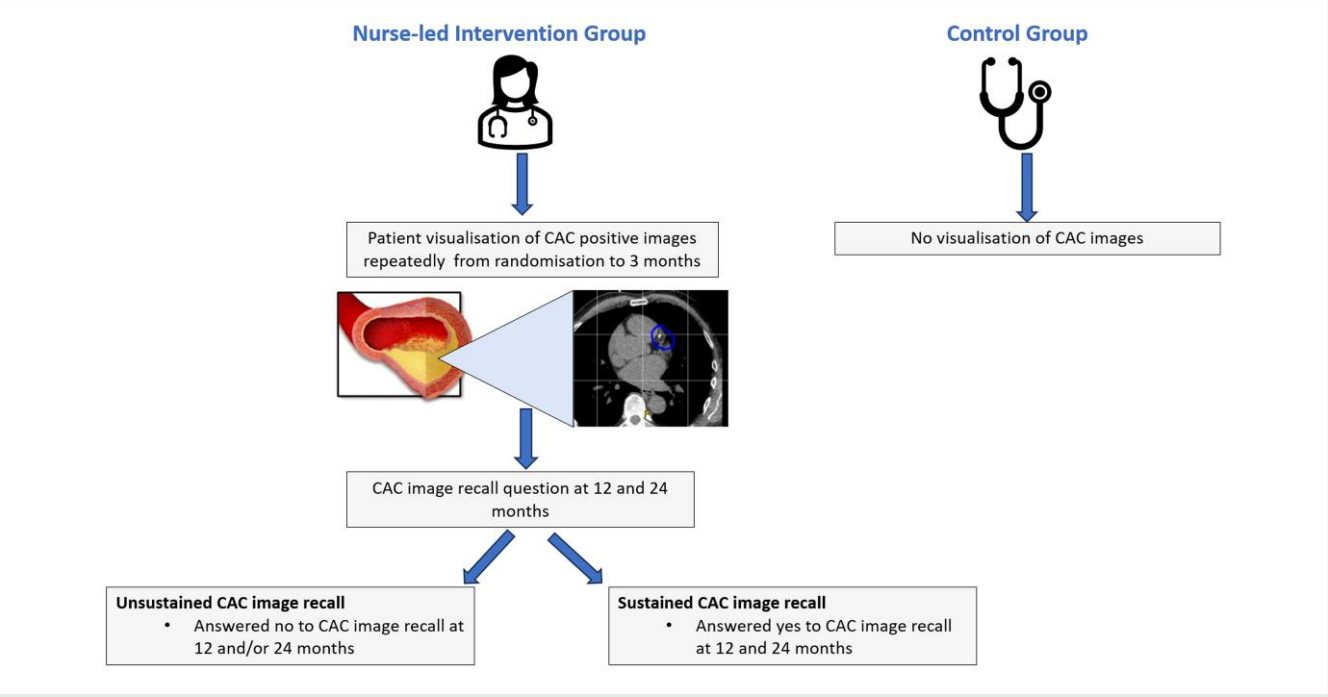

Figure 2 Coronary artery calcium image recall within the intervention group. The control group received standardized CV risk information informed by current CV prevention guidelines. Conversely, the intervention was comprised of a structured nurse-led CV risk discussion and patient visualization of CAC images depicting subclinical coronary atherosclerosis along with their CAC score. The intervention group at 12 and 24 months was asked a specific question at the beginning of the visit regarding recall of their recollection of CAC images: 'do you remember seeing the CAC image?'. Sustained recall was defined as self-reported recall of their CV image at 12- and 24-month visits, whereas unsustained recall was defined as not recalling their CAC image at either or both of 12- and 24-month visits. These responses were used to assess the influence of recall of CV images on changes in FRS and CV risk factors from baseline to 36-month follow-up. CAC, coronary artery calcium; CV, cardiovascular; FRS, Framingham Risk Score.

software, Version 15.0 (StataCorp. 2017. College Station, TX: StataCorp LLC) and R.

Results

Study cohort

The baseline characteristics of the study population of 449 individuals with 229 in the control group and 220 in the intervention group. The baseline characteristics were generally well balanced between the intervention and control groups, albeit there were more participants with diabetes mellitus in the control group (7 vs. 1, $P = 0.04$) (*Table 1*).

Of the 449 individuals, 407 participants (91%) completed the 36-month follow-up (*Figure 1*). Those with early withdrawals over the 36 months in the control group ($n = 11$) and the intervention group ($n = 17$) were mainly due to participant choice and lost to follow-up (no response). The 36-month follow-up had a small percentage of missing data for the FRS (10%). The 12- and 24-month follow-up was disrupted due to the COVID-19 pandemic in 20% and 64% of participants, respectively. The 24-month fasting cholesterol profiles were only available for 107 participants in intervention and 86 participants in usual care impacting on analysis for CV risk (*Figure 1*). Adherence to statin therapy in the intervention group was maintained at 36 months with 89% reporting daily usage (158/178). There was 13% participants in the control group (29/229) who reported daily use of primary care-initiated statin therapy at 36 months.

Primary outcome

The median FRS was 11.1% in the control group and 11.3% (*Table 1*) in the intervention group at baseline. The absolute change of FRS at 36 months was significantly lower in the intervention group (DID −3.4%; [95% CI: −4.4% to −2.4%], $P < 0.001$) vs. the control group (*Table 2* and Supplementary material online, *Table S1*). The subgroup analyses found no significant interaction between any stratification variable and study intervention on the change in the primary outcome (see Supplementary material online, *Tables S3–S5*).

The intervention group had the greatest decrease in FRS within the first 12 months, with this reduction sustained to the 36 months (*Table 2* and *Figure 3A*). Conversely, participants in the control group exhibited a slight increase in FRS at 12 months, which then reverted to levels comparable to those seen at 36 months (*Figure 3A*). Additional analysis found that the study intervention, increasing age, male sex, diabetes mellitus, baseline antihypertensive use, and high CAC score were significant predictors for FRS change over the 36-month follow-up (see Supplementary material online, *Table S6*).

Individual cardiovascular risk factors

There was a favourable impact on all CV risk factors in the intervention group. There were significant reductions in TC (DID −1.3 mmol/L [95% CI: −1.4 to −1.1], $P \leq 0.001$), LDL-C (DID −1.2 mmol/L [95% CI: −1.4 to −1.1], $P \leq 0.001$), and triglycerides (DID −0.2 mmol/L [95% CI: −0.4 to −0.1], $P = 0.003$) in the intervention group compared to the control group over 36 months (*Table 2* and Supplementary material online, *Table S3*). The greatest LDL-C and TC reduction in

Table 1 CAUGHT-CAD baseline characteristics

		Overall $n = 449$	Control $n = 229$	Intervention $n = 220$
Demographics	Age, yrs (mean, SD)	57.9 (7.1)	58.3 (7.1)	57.7 (7.0)
	Male, *n* (%)	256 (56.9)	123 (53.7)	133 (60.2)
	1st degree family history of CAD, *n* (%)	416 (93.7)	210 (93.3)	206 (94.1)
	High school or lower, *n* (%)	215 (50.1)	112 (52.1)	103 (48.1)
	Tertiary education, *n* (%)	214 (49.9)	103 (47.9)	111 (51.9)
	Systolic blood pressure, mmHg (mean, SD)	129.6 (13.1)	129.6 (12.9)	129.7 (13.3)
	Diastolic blood pressure, mmHg (mean, SD)	79.4 (9.9)	79.2 (9.6)	79.5 (10.4)
	SBP and/or DBP ≥ 140/90 mmHg (mean, SD)	119 (26.5)	64 (27.9)	55 (25.0)
	Heart rate, beats per minute (mean, SD)	68.1 (10.6)	67.2 (9.7)	68.9 (11.4)
	6 min walk, metres (mean, SD)	558.9 (77.8)	554.6 (76.2)	563.4 (79.4)
	<4 standard alcoholic drinks per week, *n* (%)	223 (50)	123 (54.2)	100 (45.7)
	≥4 standard alcoholic drinks per week, *n* (%)	223 (50)	104 (45.8)	119 (54.3)
Cardiac risk factors	Diabetes mellitus, *n* (%)[a]	8 (1.8)	7 (3.1)	1 (0.5)
	Current smokers, (*n*) %	20 (4.5)	10 (4.4)	10 (4.6)
	Waist circumference, cm (mean, SD)	94.7 (13.9)	95.0 (14.6)	94.3 (13.3)
	BMI (mean, SD)	27.6 (5.5)	27.8 (5.9)	27.5 (5.1)
Clinical laboratory values (mean, SD)	LDL cholesterol (mmol/L)	3.4 (0.7)	3.3 (0.7)	3.4 (0.7)
	Total cholesterol (mmol/L)	5.5 (0.7)	5.5 (0.6)	5.5 (0.7)
	HDL cholesterol (mmol/L)	1.5 (0.5)	1.5 (0.5)	1.5 (0.4)
	Triglycerides (mmol/L)	1.3 (0.7)	1.3 (0.8)	1.3 (0.6)
	Fasting glucose (mmol/L)	5.2 (0.6)	5.1 (0.6)	5.2 (0.6)
Medication use	Antihypertensive, *n* (%)	89 (19.8)	52 (22.7)	37 (16.8)
	Glucose lowering medication, *n* (%)	6 (1.3)	5 (2.2)	1 (0.5)
CAC results	Coronary Artery Calcium (CAC) score, median (IQR)	33.7 (7 to 100.9)	33 (6.4 to 98.3)	33.9 (8 to 102.5)
	>0–9, *n* (%)	143	75 (32.9)	68 (31.1)
	10–100, *n* (%)	191	97 (42.5)	94 (43.1)
	101–400, *n* (%)	112	56 (24.6)	56 (25.7)
Predicted CV risk	Framingham Risk Score (FRS), median (IQR)	11.2 (7.4–17.4)	11.1 (7.3 to 17.8)	11.3 (7.4 to 16.8)
	FRS < 10%, *n* (%)	226 (50.8)	114 (50.2)	112 (51.4)
	FRS 10.1–≤15%, *n* (%)	92 (20.7)	42 (18.5)	50 (22.9)
	FRS 15.1–20%, *n* (%)	69 (15.5)	33 (14.5)	36 (16.5)
	FRS > 20%, *n* (%)	58 (13.0)	38 (16.7)	20 (9.2)
	FRS (%) (mean, SD), men	16.9 (8.4)	17.9 (9.2)	15.8 (7.5)
	FRS (%) (mean, SD), women	8.6 (3.9)	8.5 (3.9)	8.7 (1.1)
Mental health and quality of life (mean, SD)[b]	Depression (PHQ-9)	1.7 (2.2)	1.9 (2.7)	1.7 (2.2)
	Anxiety (GAD-7)	1.4 (2.4)	1.5 (2.5)	1.3 (2.3)
	EQ5D-5L index score	0.97 (0.05)	0.97 (0.06)	0.97 (0.04)
	EQ5D-5L VAS	86.2 (11.2)	86.4 (11.1)	85.9 (11.4)

BMI, body mass index; CAC, coronary artery calcium; CAD, coronary artery disease; CV, cardiovascular; DBP, diastolic blood pressure; FRS, Framingham Risk Score; GAD, generalized anxiety disorder; HDL, high density lipoprotein; LDL, low density lipoprotein; PHQ9, patient health questionnaire 9; SD, standard deviation; SBP, systolic blood pressure; VAS, visual analogue scale.

[a]Diabetes mellitus was defined as self-reported diabetes mellitus, fasting plasma glucose ≥ 7 mmol/L, or use of any glucose lowering medications.

[b]Mental health and quality of life questionnaires completed by the participant; EQ5D-5L, 5-level EQ5D version quality of life survey; GAD-7, general anxiety disorder; PHQ-9, patient health questionnaire-9.

the intervention group was observed within the first 12 months and was maintained to 36 months (*Table 2*, *Figure 3B and C*, and Supplementary material online, *Tables S3–SS5*). There was no significant difference in the change in HDL-C within 36 months between the intervention and control groups (DID 0.004 mmol/L [95% CI: −0.1 to 0.1], $P = 0.941$) (*Table 2* and Supplementary material online, *Table S3*).

The reduction in SBP (DID −3.3 mmHg, $P = 0.034$) and DBP (DID −3.3 mmHg, $P = 0.006$) in the intervention group was statistically significant at 24 months, but this was not sustained at 36 months of follow-up (SBP; $P = 0.340$, DBP; $P = 0.306$) (*Table 2* and Supplementary material online, *Tables S3–SS5*). SBP and DBP mean values at each annual visit in the intervention group were consistently lower than the control group

Table 2 Impact of a nurse-led programme and visualization of coronary artery calcium images vs. control on FRS and CV risk factors annually

Variables	Baseline to 12-month mean (95% CI)	*P*	Baseline to 24-month mean (95% CI)	*P*	Baseline to 36-month mean (95% CI)	*P*
FRS (%)	−4.2 (−5.2 to −3.2)	<0.001	−4.2 (−5.5 to −2.8)	<0.001	−3.4 (−4.4 to −2.4)	<0.001
Systolic blood pressure (mmHg)	−2.5 (−5.2 to 0.1)	0.061	−3.3 (−6.3 to −0.2)	0.034	−1.5 (−4.2 to 1.1)	0.340
Diastolic blood pressure (mmHg)	−0.9 (−2.9 to 1.1)	0.356	−3.3 (−5.6 to −0.9)	0.006	−1.0 (−3.1 to 0.9)	0.306
BMI (kg/m^2)	0.5 (−0.2 to 1.3)	0.181	0.1 (−0.3 to 0.6)	0.585	0.04 (−0.5 to 0.6)	0.851
LDL cholesterol (mmol/L)	−1.4 (−1.6 to −1.2)	<0.001	−1.2 (−1.5 to −0.9)	<0.001	−1.2 (−1.4 to −1.0)	<0.001
Total cholesterol (mmol/L)	−1.5 (−1.6 to −1.3)	<0.001	−1.3 (−1.5 to −1.0)	<0.001	−1.3 (−1.4 to −1.1)	<0.001
HDL cholesterol (mmol/L)	−0.01 (−0.1 to 0.02)	0.192	−0.1 (−0.2 to 0.03)	0.178	0.0 (−0.1 to 0.1)	0.941
Triglycerides (mmol/L)	−0.2 (−0.3 to −0.03)	0.020	−0.1 (−0.3 to 0.1)	0.296	−0.2 (−0.4 to −0.1)	0.003
Current smoking (%)	−1.29 (−4.2 to 1.6)	0.380	−1.3 (−3.9 to 1.4)	0.346	−1.7 (−5.2 to 1.8)	0.344

Difference in differences in FRS and cardiovascular risk factors annually. All variables have been adjusted for baseline age, sex, and diabetes mellitus status. The absolute change of FRS over 3 years was significantly lower in the intervention group vs. the control group. There was a favourable impact within all CV risk factors in the intervention group.
CI, confidence interval; CV, cardiovascular; BMI, body mass index; FRS, Framingham Risk Score; LDL, low density lipoprotein.

(*Figure 3D* and *E*). There were no statistically significant effects for the remaining CV risk factors (*Figure 3F* and Supplementary material online, *Tables S3–SS5*).

Psychological safety measures and lifestyle behaviours

Intervention did not increase the health status, depression, and anxiety scores over the 36 months follow-up (see Supplementary material online, *Table S7*). The benefits of the intervention on daily exercise and health adherence only became apparent at 36 months ($P \leq 0.001$) (see Supplementary material online, *Table S8*).

Impact of sustained recall of coronary artery calcium images

An exploratory analysis within the intervention group focused on 130 participants classified as those with sustained CV image recall and 66 as unsustained CV image recall (*Figure 2*). There was no significant impact of sustained CV image recall from baseline to 24 months on the change of FRS during the 36-month follow-up (sustained vs. unsustained: DID −0.8% [95% CI: −1.9 to 0.4], $P = 0.20$) (*Figure 4* and Supplementary material online, *Table S9*). A significant reduction in SBP (DID −4.3 mmHg [95% CI: −7.7 to −0.9], $P = 0.01$) and WC (DID −2.0 cm [95% CI: −3.9 to −0.1], $P = 0.03$) was observed in the sustained recall of CAC image group vs. the unsustained CAC image group (*Figure 4*). There were no statistically significant effects for the remaining CV risk factors.

Discussion

This study sought to determine whether patient visualization of personalized CAC images is an effective tool within a structured nurse-led programme to sustain long-term CV risk control in primary prevention. The results from this study demonstrated that repeated exposure to personalized CAC images and statin use within a nurse-led programme was associated with sustained improvements in FRS, SBP, and WC up to 36 months. The visual representations depicting coronary atherosclerosis, achieved by highlighting the pathology, were repeatedly utilized during the discussion on CV risk within the first 3 months post-randomization. The CAC images offered tangible evidence of subclinical pathology.[19] To the best of our knowledge, this is the first study that used recall of pictorial images of coronary atherosclerosis in an intermediate-risk population with a family history of premature coronary artery disease to motivate adherence to primary prevention strategies.

The use of CV images to communicate risk has been shown to improve predicted CV risk through improved adherence to lifestyle management and preventive therapies, however caution must be exercised due to complications arising from significant heterogeneity in study design.[12,20–22] A recent meta-analysis on the impact of patient visualization of cardiovascular images on modification of CV risk factors observed a greater reduction in risk seen in those who had atherosclerosis (−1.59%) vs. those without atherosclerosis (−0.41%).[13] The meta-analysis included only three RCTs that utilized CAC to detect coronary atherosclerosis. The novelty of this trial is that it is first RCT looking at the usefulness of CAC imaging in intermediate-risk individuals with subclinical coronary atherosclerosis and a family history of premature coronary artery disease. This trial is also the first RCT that allocated statin therapy to the intervention group, with a longer follow-up of 3 years. The 12-month follow-up of this study reported a difference in the change of FRS between the intervention and control groups of −4.2% which we found was sustained at 36 months with a difference of −3.4%. This sustained significant improvement in predicted CV risk could be attributed to the novel use of a nurse-led programme that combined patient visualization of CAC imaging within the CV risk discussion. This is also supported by the participants' high adherence rate to statin therapy at the end of follow-up. The implementation of a nurse-led programme in this study provided individuals in both the control and intervention groups with focused CV reviews every 6 months. The intervention group underwent multiple exposures to their personalized CV images, aiming to create a 'teachable moment' that would boost their motivation to initiate change.[9,23] Individuals who

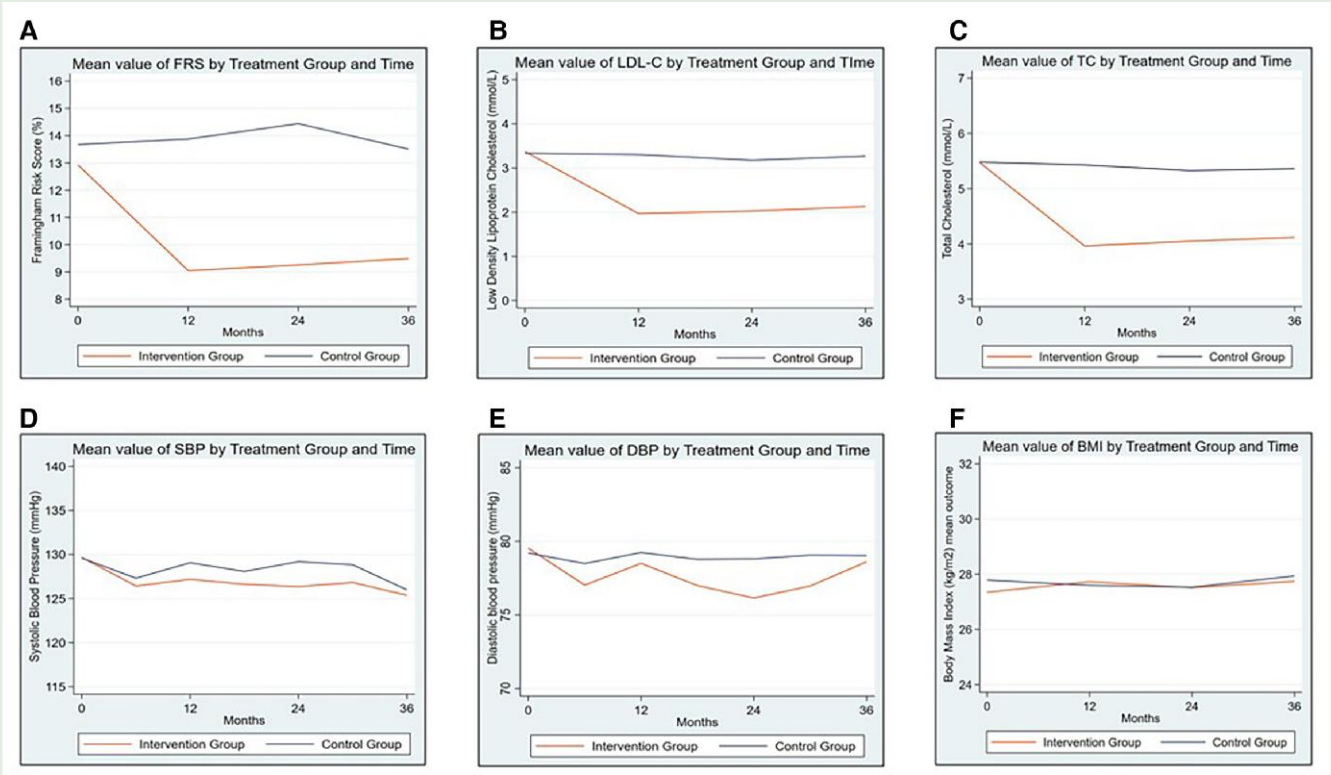

Figure 3 Mean change in Framingham Risk Score and cardiovascular risk factors from baseline to 36 months. Panel *A* is the mean value of FRS by treatment group and time. The intervention group had the greatest decrease in FRS within the first 12 months, with this reduction sustained to the 36 months. Conversely, participants in the control group exhibited a slight increase in FRS at 12 months, which then reverted to levels comparable to those seen at 36 months. Panels *B* and *C* are the mean values for LDL-C and TC by treatment group and time. The greatest LDL-C and TC reduction in the intervention group was observed within the first 12 months and was maintained to 36 months. Panels *D* and *E* are the mean values for SBP and DBP by treatment group and time. SBP and DBP mean values in the intervention group were consistently lower than the control group throughout the 36-month follow-up. Panel *F* is the mean value of BMI by treatment group and time. No difference in BMI was observed between the intervention and control groups during the 36-month follow-up. FRS, Framingham Risk Score; BMI, body mass index; DBP, diastolic blood pressure; LDL-C, low density lipoprotein cholesterol; SBP, systolic blood pressure; TC, total cholesterol.

were exposed to the CV image guided care (intervention group) and recalled their CAC image up to 24 months follow-up observed a significant reduction in SBP and WC at 36 months compared to those who could not recall their CAC image. The sustained recollection of visualizing coronary plaque in the absence of symptoms may have acted as a catalyst, motivating those individuals to adhere to primary prevention strategies. The non-significant findings of FRS and lipid profile between sustained and unsustained CAC image recall can be attributed to the high rate of adherence to statin therapy within the CV image guided group. VIPVIZA is a randomized trial with a similar study design, where the aim was to determine whether participant visualization of carotid ultrasound images improves adherence to CV primary prevention strategies.[20,24] Although the VIPVIZA trial did not report on individual recall of CV images throughout the follow-up, the constant exposure to the images may have influenced the beneficial effect on cardiovascular risk observed in the intervention vs. control group at 36 months.[20]

One of the concerns with more active supervision, and especially with providing plaque images, is that provision of this information may negatively impact the individual's mental wellbeing and cause undue harm following the knowledge regarding the presence of coronary plaque.[25] An increase in worry has been posited by previous observational research following the individual's knowledge of their CAC results.[26,27] In this study, health-related quality of life, depression, and anxiety scales showed no difference between control and intervention group participants at baseline and 36 months. The results are consistent with an observational study that showed no change in worry scores 3 months following CAC screening.[9] These findings imply that individuals demonstrate competence in handling the information acquired from their awareness of their CAC score, without detriment to their psychological health.

Although the 36-month follow-up of our study did not observe significant reductions in the secondary outcomes (other than cholesterol measures), there was a modest reduction in SBP for participants in both the control and intervention groups at 36 months. DBP and BMI measurements at the 36-month follow-up were similar to baseline for both control and intervention. These findings could be due to both randomized groups receiving nurse involvement with the purpose of ensuring that even those allocated to the control group received discussions about modifiable CV risk factors that went beyond the basic level of care. Both groups were reviewed by experienced research nurses within the structured programme, and this may have influenced the control group to actively modify their CV risk factors. A similar nurse coordinated programme with a focus on cardio-metabolic risk reduction (the MODERN trial[28]) produced similar, risk factor changes with no

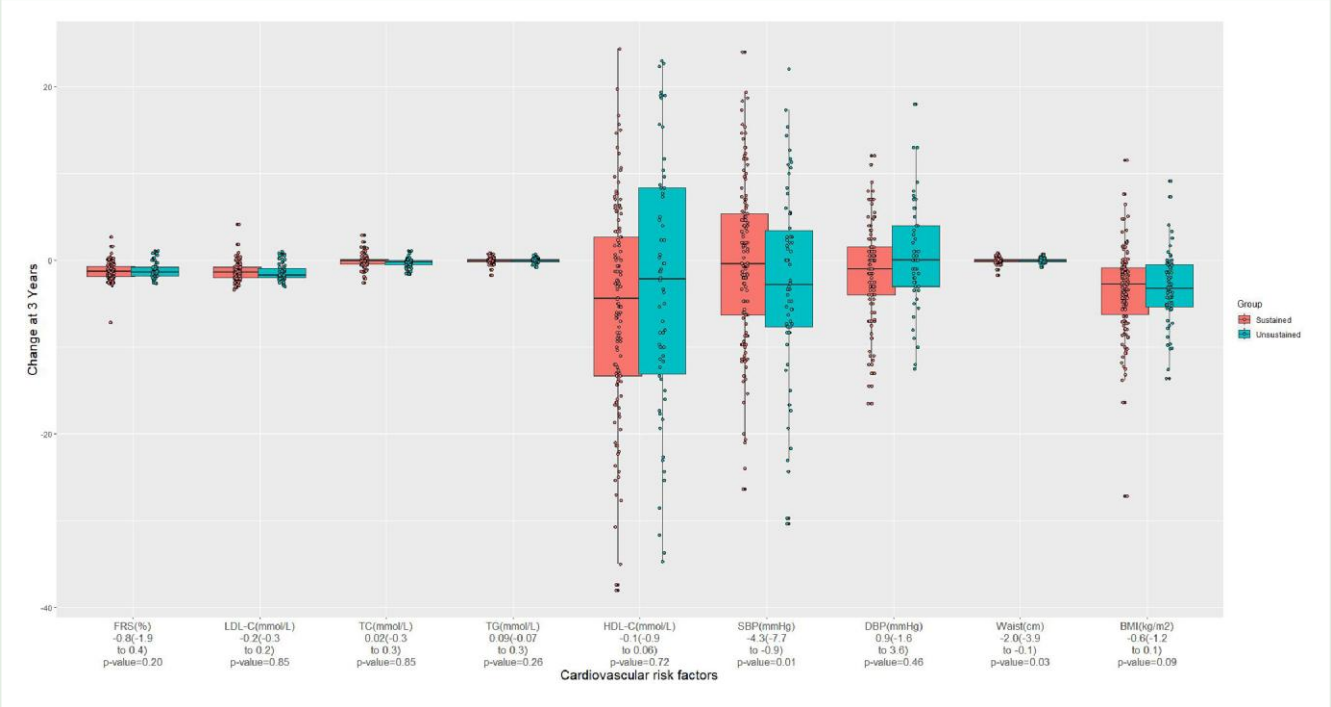

Figure 4 Impact of unsustained vs. sustained recall of CAC images on change in FRS and CV risk factors at 3 years. There was no significant impact of sustained CV image recall from baseline to 24 months on the change of FRS during the 36-month follow-up (sustained vs. unsustained: DID −0.8% [95% CI: −1.9 to 0.4], $P = 0.20$). A significant reduction in SBP (DID −4.3 mmHg [95% CI: −7.7 to −0.9], $P = 0.01$) and waist circumference (DID −2.0 cm [95% CI: −3.9 to −0.1], $P = 0.03$) was observed in the sustained recall of CAC image group vs. the unsustained CAC image group. There were no statistically significant effects for the remaining CV risk factors. CI, confidence interval; DID, difference in differences; FRS, Framingham Risk Score; BMI, body mass index; CV, cardiovascular; DBP, diastolic blood pressure; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; SBP, systolic blood pressure; TC, total cholesterol; TG, triglycerides.

intervention group effects, perhaps attributable to the Hawthorne effect.[29]

Healthcare providers continue to face challenges in achieving optimal adherence to primary pharmacotherapy and lifestyle modification in the prevention of CV disease.[8,30] Once strategies such as primary pharmacotherapy and lifestyle modification are implemented, long-term adherence becomes arduous.[5,8,25] Irrespective of socioeconomic status and level of education, the intervention group in our study demonstrated consistently high adherence to statin therapy during each of the annual reviews. Individuals regardless of sustained or unsustained CAC image recall remained adherent to statin therapy (~87%) throughout the 36-month follow-up. The observed high adherence can be attributed to the nurse-led programme, which likely emphasized the potential threat of CV disease. Adherence to statin therapy remains a mainstay for primary prevention of CV disease.[4,8,31,32] Early initiation of statin therapy to aggressively lower LDL-C levels in those with a family history of premature coronary artery disease and subclinical coronary atherosclerosis is imperative to achieve sustained benefits in CV outcomes.[4,8,30,31]

The study findings underscore the efficacy of a structured nurse-led programme in supporting and promoting long-term adherence to statin therapy. These results for FRS were reported irrespective of whether plaque images were recollected by patients, albeit with better SBP control in those who did recollect the imaging findings. The successful programme could be expected to lead to a reduction in the incidence of CV disease and improved cardiovascular health among at-risk individuals.

Limitations

Research nurses were not blinded to randomization due to logistical impracticalities, precluding the implementation of a double-blind methodology. Due to unblinded nature of the study design, this may have influenced the outcomes in the control group producing similar risk factor changes with no intervention group effects. Twenty-four-month outcome data were disrupted due to the global COVID-19 pandemic. The research staff gained secondary outcome data during lockdown through the utilization of telehealth, which was a departure from the trial protocol. Despite this, telehealth has shown its value in adjusting risk factors and promoting consistent adherence to pharmacotherapy for the management of CVD.[33,34] The analysis of the 24-month data is constrained by substantial missing data, amounting to 62.5% and 48.6% in the control and intervention groups, respectively. However, the implementation of telehealth led to a notable reduction in missing data for the 24-month secondary outcome, decreasing to 19% in the control group and 15% in the intervention group. Nevertheless, the utilization of telehealth might have introduced a bias, as it necessitates access to Wi-Fi and mobile phones, although the missing data appears to be random and not restricted to specific key populations. The CAC image recollection query involved a straightforward binary response, requiring a 'yes' or 'no' answer at both the 12- and 24-month intervals with no comparative data from the control group. Although these data were used to project change in primary and secondary outcomes at 36 months, the interpretation of the data is limited. Future research should focus on isolating the influence of the CAC image within discussions regarding CV risk modification. The robustness of the self-reported

adherence to a healthy diet and exercise in this study allowed for participant interpretation, potentially limiting the generalizability of results. This study lacked information on the specific nature of the exercise, the intensity level, and duration (in minutes), which are crucial factors for evaluating the influence of this important modifiable risk factor.

Conclusion

Repeated exposure to personalized CAC images coupled with a CV risk discussion and the implementation of statin therapy within a structured nurse-led programme is associated with significant improvements in predicted CV risk. This multifaceted approach is further associated with notable improvements in SBP and WC.

Collaborators

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Supplementary material

Supplementary material is available at *European Journal of Preventive Cardiology*.

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Author contribution

Authorship K.W. and T.H.M. contributed to the conception or design of the work. Z.Z., M.J.C., and C.G.M. contributed to the acquisition, analysis, or the interpretation of the data for the work. K.W. drafted the manuscript. T.H.M. and M.J.C. critically revised the manuscript. All gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

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Data availability

The corresponding author is willing to provide the underlying data for this research paper upon a reasonable request.

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