Supplementary data

Supplementary Appendix 1. Study Committees.

Steering Committee:

Shamir Mehta (Principal Investigator, Chair), McMaster University, Hamilton Health Sciences, Population Health Research Institute, Hamilton, ON, Canada

Eva Lonn, McMaster University, Hamilton Health Sciences, Population Health Research Institute, Hamilton, ON, Canada

Guillaume Pare, McMaster University, Hamilton Health Sciences, Population Health Research Institute, Hamilton, ON, Canada

Matthew McQueen, McMaster University, Hamilton Health Sciences, Population Health Research Institute, Hamilton, ON, Canada

Data Safety Monitoring Committee:

Shaun Goodman (Chair), University of Toronto, St. Michael's Hospital, Toronto, ON, Canada, and University of Alberta, Edmonton, AB, Canada

Todd Anderson, University of Calgary, Calgary, AB, Canada

Jacques Genest, McGill University, Montreal, QC, Canada

Supplementary Appendix 2. Methods: pre-analytical and analytical process.

Specimens were collected, transported to the central lab (CRLB-GMEL), and processed within 2 hours of collection. After processing, samples were stored in liquid nitrogen vapor (-165°C) until analysis.
Prior to analysis, specimens underwent controlled thaw and vortexing. Samples were analyzed within 1 hour of thaw, or placed in the refrigerator.

Supplementary Table 1. Analytical methods.

Analyte	Manufacturer	Instrument	Method
Direct LDL	Beckman Coulter	Unicel DxC 600	Automated colorimetric timed-endpoint
Cholesterol	Beckman Coulter	Unicel DxC 600	Automated colorimetric timed-endpoint
HDL	Beckman Coulter	Unicel DxC 600	Automated colorimetric timed-endpoint
Trig	Beckman Coulter	Unicel DxC 600	Automated colorimetric timed-endpoint (glycerophosphate oxidase)
ApoB	Beckman Coulter	Unicel DxC 600	Automated turbidimetric (antibody/antigen complex)
Lp(a)	Roche/Randox	Cobas 6000	Automated immunoturbidimetric
CRP	Beckman Coulter	Unicel DxC 600	Automated turbidimetric (antibody/antigen complex)
CKMB	Roche	Cobas 8000	Automated ECLIA (electrochemiluminescence immunoassay)

Direct LDL

The method depends on a unique detergent which solubilizes only the non-LDL lipoprotein particles and releases cholesterol to react with cholesterol esterase and cholesterol oxidase to produce a non-colour forming reaction. A second detergent solubilizes the remaining LDL particles, and a chromogenic coupler allows for colour formation.
LDLD reagent is used to measure the cholesterol concentration by a timed-endpoint method. The Beckman Coulter Synchron System(s) automatically proportions the appropriate LDL cholesterol sample and reagent volumes into a cuvette. The ratio used is one part sample to 93 parts reagent. The System monitors the change in absorbance at 560 nanometers. This change in absorbance is directly proportional to the concentration of LDL cholesterol in the samples and is used by the System to calculate the express the LDL cholesterol concentration.

Supplementary Table 2. Baseline characteristics (included vs excluded).

	Included	**Excluded**	
	Mean (SD)	**Mean (SD)**	**p-value**
	N=68	N=29	
Age (yrs)	62.37 (10.74)	65.48 (14.14)	0.24
BMI	28.98 (5.60)	28.29 (5.42)	0.59
Systolic blood pressure (mm/Hg)	144.1 (23.79)	148.9 (23.47)	0.36
Diastolic blood pressure (mm/Hg)	89.22 (15.80)	87.31 (16.21)	0.59
Heart rate (bpm)	88.84 (23.89)	88.17 (29.92)	0.91
Male	55 (80.88)	20 (68.97)	0.29
White	61 (89.71)	26 (89.66)	1.00
Current smoker	23 (33.82)	14 (48.28)	0.18
Medical history			
Previous MI	6 (8.82)	4 (13.79)	0.48
Previous stroke	1 (1.47)	0 (0.00)	1.00
Family history of early onset coronary artery disease	7 (10.29)	3 (10.34)	0.99
Atrial fibrillation/flutter	2 (2.94)	0 (0.00)	0.35
History of heart failure	0 (0.00)	0 (0.00)	---
Peripheral arterial disease	1 (1.47)	1 (3.45)	0.53
Hypertension	30 (44.12)	13 (44.83)	0.95
Dyslipidemia	25 (36.76)	9 (31.03)	0.59
Diabetes	6 (8.82)	4 (13.79)	0.46
Chronic renal insufficiency	0 (0.00)	0 (0.00)	---
Other relevant ongoing medical condition	10 (14.71)	5 (17.24)	0.75
Time from symptom onset to primary PCI	3.65 (2.25)	3.28 (2.07)	0.46
Prior statin use	16 (23.53)	1 (3.45)	0.02

Supplementary Table 3. Baseline measurements (included vs excluded).

	Included	Excluded	p-value
N	68	29	.
LDL-cholesterol (mmol/L), mean(SD)	2.92 (1.01)	2.89 (1.10)	0.88
ApoB (g/L), mean(SD)	0.86 (0.30)	0.85 (0.31)	0.91
Non HDL-cholesterol (mmol/L), mean(SD)	3.58 (1.22)	3.46 (1.31)	0.67
Total cholesterol (mmol/L), mean(SD)	4.63 (1.21)	4.58 (1.35)	0.87
Triglycerides (mmol/L), median(IQR)	1.09 (0.63, 1.62)	0.92 (0.60, 1.36)	0.29
HDL-cholesterol (mmol/L), mean(SD)	1.04 (0.28)	1.12 (0.28)	0.25
Lp (a) (mg/L), median(IQR)	73 (34, 427)	158 (47, 447)	0.41

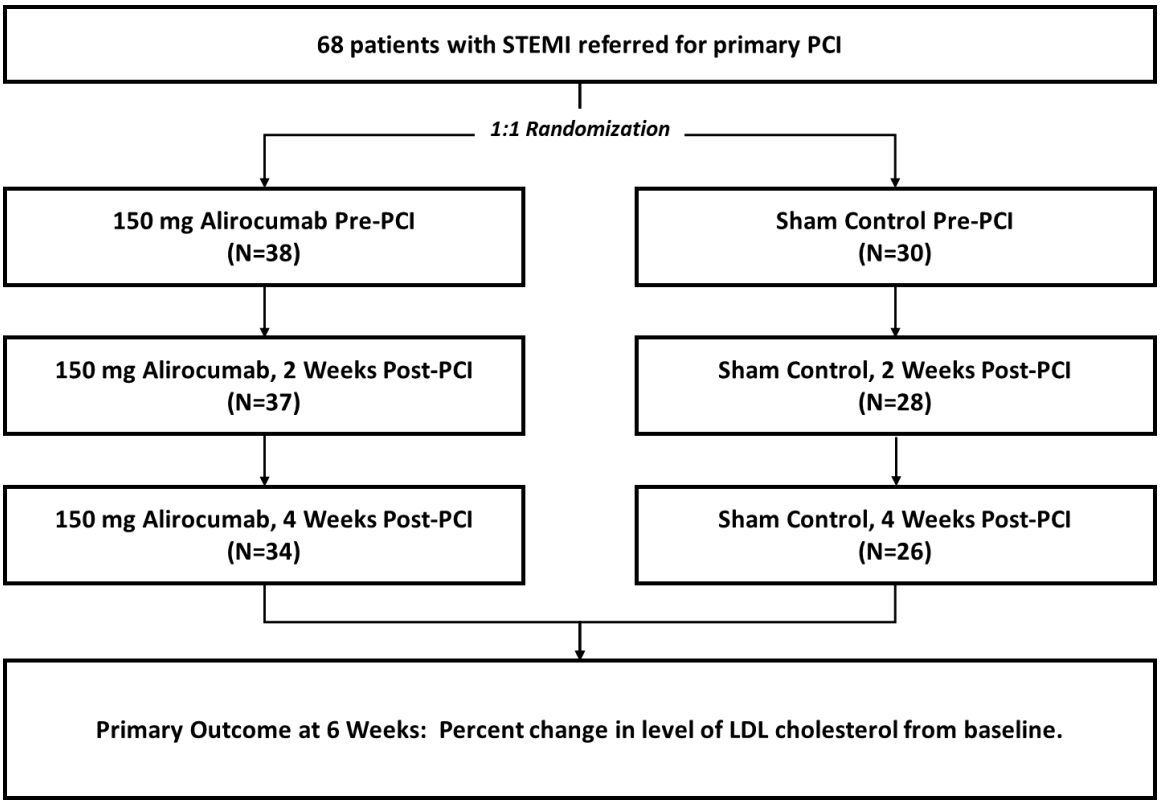
Supplementary Table 4. LDL- and ApoB-adjusted analyses with gender.

	Alirocumab N=38			**Sham Control N=30**			**Between Group Difference (95% CI)**	**P**
	Baseline	**Follow-up**	**Percent Change**	**Baseline**	**Follow-up**	**Percent Change**		
LDL-cholesterol (mean [SD], mmol/L)	2.97 (1.09)	0.75 (0.46)	-72.9% (17.5)	2.87(0.90)	1.30 (0.45)	-48.1% (29.5)	-23.7% (-32.7, -14.7)	<0.001
ApoB (mean [SD], g/L)	0.88 (0.33)	0.40 (0.11)	-50.6(17.7)	0.83 (0.25)	0.49 (0.13)	-36.3 (24.4)	-12.2 (-18.7, -5.7)*	<0.001

*68.4% of patients in the alirocumab group versus 26.7% in the sham control group had ApoB levels ≤ the assay lower detection limit of 0.35 g/L (P=0.001). All of these patients were assigned a value of 0.35 g/L.

Supplementary Table 5. Adverse events.

Event	Treatment Allocation	Summary
Death	Sham Control	Death reported 11 days post 1st injection. Unknown cause.
Heart failure	Alirocumab	Heart failure reported 2 days post 1st injection.
Heart failure	Alirocumab	Heart failure reported 2 hours post 1st injection.
Heart failure	Alirocumab	Heart failure reported 1 hour post 1st injection.
Heart failure	Alirocumab	Heart failure reported 2 days post 1st injection.
Minor bleeding	Sham Control	Minor bleeding reported 48 days post 3rd injection.



Supplementary Figure 1. Trial flow diagram.