TITLE PAGE

Title: Efficacy of a Nurse-Led Lipid-Lowering Secondary Prevention Intervention in Patients Hospitalized for Ischemic Heart Disease: A Pilot Randomized Controlled Trial

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ABSTRACT

Background

Lack of achievement of secondary prevention objectives in patients with ischemic heart disease (IHD) remains an unmet need in this patient population.

Aims

We aimed at evaluating the 6-month efficacy of an intensive lipid-lowering intervention, coordinated by nurses and implemented after hospital discharge, in patients hospitalized for an IHD event.

Methods

Pilot randomized controlled trial enrolling 78 patients (39 in each arm). A nurse-led intervention including follow-up, serial lipid level controls, and subsequent optimization of lipid-lowering therapy, was compared to standard of care in terms of serum lipid-level control at 6 months after discharge.

Results

The nurse-led intervention was associated with an improved management of LDL cholesterol levels compared to standard of care alone: LDL cholesterol levels ≤100 mg/dL were achieved in 97% participants in the intervention arm as compared to 67% in the standard care arm (p value <0.001), the LDL cholesterol ≤70 mg/dL target recommended by the 2016 European Society of Cardiology guidelines was achieved in 62% vs 37% participants (p value 0.047), and the LDL cholesterol reduction ≥50% recommended by the American College of Cardiology/American Heart Association in 2013 was achieved in 25.6% participants in the intervention arm as compared to 2.6% in the standard care arm (p value 0.007). The intervention was also associated with improved blood pressure control among individuals with hypertension.

Conclusions

Our findings highlight the opportunity that nurse-led, intensive, post-discharge follow-up plans may represent for achieving LDL cholesterol guideline-recommended objectives in patients with IHD. These findings should be replicated in larger cohorts.

ABBREVIATIONS AND ACRONYMS

CRP	cardiac rehabilitation program
ESC	European Society of Cardiology
EUTERPE	Estudio de UTilización del chronic care model en pacientes isquémicos de Elevado Riesgo mediante un Proceso basado en Enfermería (Spanish acronym)
IHD	ischemic heart disease
LDL	low density lipoprotein
NSTEMI	non-ST elevation myocardial infarction
STEMI	ST elevation myocardial infarction

TEXT

Introduction

Despite landmark primordial and primary preventive efforts,[1,2] as well as dramatic improvements in the acute-phase care of ischemic heart disease (IHD) patients attained in the last three decades,[3–5] IHD remains one of the leading causes of death worldwide.[5,6]

Among the prevailing unmet needs in the care of these patients, lack of achievement of secondary prevention targets after an acute IHD event is currently considered a key issue.[7,8] Specifically, although the guidelines of the European Society of Cardiology (ESC) recommend that patients with overt IHD should be treated aggressively to achieve low density lipoprotein (LDL) cholesterol levels ≤70 mg/dL,[7,9] this treatment goal is often not achieved.[8] Poor adherence to lifestyle recommendations and pharmacological therapies by patients[10], as well as time constrains, limited follow-up and medication titration by healthcare providers are considered important participating factors.[11–13]

Studies suggest that specialized post-discharge follow-up by trained nurses represents an opportunity to improve the care and outcomes of patients with cardiovascular diseases.[14–16] Nurses may have more availability than physicians to conduct close follow-up, and may communicate with patients more effectively, particularly in terms of health education. Specifically, follow-up by specialized nurses has become a key component of chronic disease management programs for patients with chronic diseases, such as heart failure.[14] However, whether this approach may also be beneficial for patients with IHD is less understood.

Our aim was thus to evaluate the 6-month efficacy of an intensive lipid-lowering intervention, coordinated by a nurse and implemented after hospital discharge, in patients hospitalized for an IHD event. For this purpose, we conducted a randomized, controlled trial in

which this intervention was compared to the standard of care, in terms of use of lipid-lowering therapies and lipid-level control at 6 months after discharge.

Materials and Methods

Study context

Since 2007, a multi-disciplinary cardiac rehabilitation program (CRP) is in place in our center. The CRP is coordinated by nurses and includes interventions performed by cardiologists, nurses, rehabilitation physicians, physiotherapists, and mental health professionals. All patients discharged from our center after a hospitalization for an acute IHD event and with no severe cognitive impairment are invited to the CRP; of them, those willing to participate enter the program. As part of the program activities, nurses educate patients in healthy habits during the in-hospital stage as well as in follow-up visits at 3 and 12 months after discharge; monitor quality of life, anxiety and depression symptoms using validated tests; and coordinate the follow-up plan. Rehabilitation physicians and physiotherapists assess the functional status of the patient and recommend and supervise physical activity during follow-up. All professionals involved in the CRP participate in monthly group sessions aimed at reinforcing the health education of the patients, with a special focus on increasing the patients' understanding of the pathophysiology of IHD and on the importance of optimal risk factor management, particularly through physical activity and adherence to pharmacotherapies. Because of its characteristics, the CRP provides an excellent platform to implement additional secondary prevention interventions.

Trial design and study participants

The **E**studio de **UT**ilización del chronic care model en pacientes isquémicos de **E**levado **R**iesgo mediante un **P**roceso basado en **E**nfermería (EUTERPE, Spanish acronym) study was a

single-center, unblinded, randomized controlled pilot trial assessing the efficacy and safety of a specialized, nurse-guided, lipid-lowering intervention aimed at improving the management of LDL cholesterol levels and other cardiovascular risk factors in patients hospitalized for IHD.

Between April 1st, 2012 and February 28th, 2013, all patients hospitalized for IHD in our center meeting inclusion criteria in the local CRP and willing to participate in the program, were screened for inclusion in this study. This included patients hospitalized for ST-segment elevation and non ST-segment elevation myocardial infarction (STEMI and NSTEMI, respectively), unstable angina, and stable angina. Of them, all patients providing written informed consent were included in the EUTERPE. The study was approved by the Ethics Committee of the Hospital del Mar and was conducted in accordance with the Declaration of Helsinki.

Interventions

Participants were randomized in a 1:1 ratio to two management arms (**Figure 1**). The "standard care arm" involved usual post-discharge follow-up, which in our healthcare area typically involves follow-up by the patient's primary care general physician, plus follow-up by a primary care cardiologist for a limited period of time; and inclusion in the standard CRP (see *Study Context* for more details).

On the other hand, the "intervention arm" involved usual post-discharge follow-up, inclusion in the standard CRP, plus the following additional interventions: 1) follow-up by a CRP nurse, who coordinated all "intervention arm" actions; 2) conduct of serum lipid level controls at months 3 and 6 after discharge; 3) evaluation of laboratory test results using a pre-specified algorithm based on clinical practice guidelines and developed ad-hoc for this study (**Supplementary Figure S1**); 4) prescription and dispensing of any additional / alternative lipid lowering treatment, if indicated according to the algorithm, by a cardiologist involved in the

CRP; and 5) communication at three and six months with the patient and with the patient's primary care physician (phone, e-mail) regarding any laboratory test results and therapeutic changes during the intervention.

Randomization to the two study arms was performed using a computer-generated randomization scheme. Study participants and personnel were aware of, i.e. not blinded to, the study intervention.

Study endpoints

The primary study endpoint was the proportion of patients with serum LDL cholesterol levels ≤70 mg/dL at 6 months of follow-up in each study arm, which is the treatment goal supported by current ESC guidelines.[7,9] Other variables related to lipid management assessed at 6 months included lipid-lowering medication use at 6 months, changes in lipid-lowering medication, changes in lipid levels as compared to hospital discharge, and proportion of individuals with a reduction in LDL cholesterol ≥50%, among others. In 2012, atorvastatin was the mostly used high intensity statin in our center. For patients treated with other statins, the atorvastatin equivalent daily dose was calculated using an equivalence chart generated by clinical pharmacy specialists.

As other secondary study endpoints, we also assessed the impact of the intervention in terms of control of other cardiovascular risk factors: proportion of patients with systolic blood pressure <140 mmHg and diastolic blood pressure <90mmHg at 6 months; proportion of patients in which blood-pressure medication had changed at 6 months compared to discharge; levels of glycosilated haemoglobin (HbA1c); and proportion of active smokers (all after 6 months of follow-up). Although these are not directly related to the study intervention, which was focused on lowering LDL cholesterol, we hypothesized that a greater number of contacts with specialized

nurses would lead to an improved management also of other risk factors. As tertiary study endpoints, we also assessed the frequency of urgent hospitalization and of all-cause death after 6 months of follow-up.

Because the safety of achieving LDL cholesterol levels <70mg/dL and of aggressive LDL cholesterol management has been largely described in the literature,[2,17,18] no safety endpoints were evaluated in this pilot analysis.

Sample size

Although initially, based on local event rates as well as on the RCT-based effect of statins in LDL cholesterol levels we estimated a sample size of 118 participants (59 per study arm using a 1:1 randomization) for the present study to have sufficient statistical power, in an interim analysis (conducted when 96 patients had already been screened for inclusion, 78 of them accepting inclusion in the study [39 patients per arm]), we already observed statistically significant differences between the two study groups in terms of the primary endpoint. Based on this, and in a context of funding limitations for the study, we decided to finalize the study recruitment.

Statistical analyses

Baseline characteristics of the study participants were described using number and proportion for categorical variables, and median (interquartile range) for continuous variables. Differences between the two study arms were compared using chi-square statistics or Fisher's exact test for categorical variables, as needed, and non-parametric tests for continuous variables in order to account for the small sample size. The same tests were used to compare the two study arms after 6 months of follow-up. There were no losses to follow-up during the study period, and no cross-overs between study arms happened either.

The absolute atorvastatin dose change at 6 months and the absolute change in LDL cholesterol levels at 6 months were described graphically, for both study arms.

All statistical analyses were performed using Stata Version 15.0.[19] A p value of <0.05 was used to define statistical significance.

Results

Study participants

Between April 1st, 2012 and February 28th, 2013, 96 IHD patients discharged after an IHD-related hospitalization met the inclusion criteria of the CRP, and were therefore screened for inclusion in the study. Of them, 78 provided written informed consent, while 18 refused participating in the study. The 78 patients included in the study were randomized in a 1:1 ratio to either the standard care arm or to the study intervention arm (N = 39 each). **Figure 1** displays the flow of the patients included in the study.

Baseline characteristics

The baseline characteristics of the study participants (i.e., at hospital discharge) are summarized in **Table 1**. Overall, the median age of the study population was 61 years, and 83% were male. There were no statistically significant differences between the 2 study groups in terms of baseline sociodemographic characteristics and other cardiovascular risk factors, in the reason for hospitalization, or in laboratory test results at admission. This included identical median baseline LDL cholesterol levels (103 mg/dL in both arms). There was a trend towards a higher median HbA1c in the intervention arm (6.1% as compared to 5.7% in the standard care arm) although this was not statistically significant.

At hospital discharge, 100% of patients in the intervention arm and 97.4% patients in the standard care arm received statins, with atorvastatin being the most frequently used option. The median equivalent daily dose of atorvastatin was identical in the two groups (40mg per day).

Lipid-lowering management and lipid level endpoints at 6 months of follow-up

Table 2 summarizes the study results in terms of lipid management at 6 months after discharge. Briefly, although statin use remained very high in both study arms, the equivalent daily dose of atorvastatin was higher in the intervention group (**Figure 2A**), and use of ezetimibe was more frequent among the patients in the intervention arm. Median total and LDL cholesterol levels were lower in the intervention arm, and the relative change in LDL cholesterol levels at 6 months was larger in the intervention arm than in the standard care arm (-36% reduction vs -26% reduction) (p 0.025). The distribution of absolute changes in LDL levels by study arm is presented in **Figure 2B**.

In this context, the primary study endpoint (proportion of patients with LDL ≤70mg/dL at 6 months of follow-up) was achieved more frequently in the intervention arm (62%) than in the standard care arm (37%) (p 0.047). The less strict target of LDL cholesterol <100 mg/dL was achieved by 97.3% and 66.7% of participants, respectively (p<0.001). Also, a LDL-cholesterol reduction ≥50% was more frequently attained in the intervention arm compared to the standard care arm (26% vs 3%) (p value 0.007).

Management of other cardiovascular risk factors

Table 3 summarizes the management of other relevant cardiovascular risk factors at 6 months of follow-up. Compared to the standard care arm, there was a trend towards a better management of blood pressure levels (systolic and diastolic blood pressure simultaneously meeting pre-specified targets) in the intervention arm compared to the standard care arm,

diastolic blood pressure levels being significantly lower in the intervention arm. When only individuals with a prior diagnosis of hypertension were compared, the frequency of patients simultaneously meeting systolic and diastolic blood pressure targets was also significantly higher in the intervention arm. On the other hand, no differences were observed between study arms with regards to tobacco use at 6 months or HbA1c levels.

Clinical events

Table 3 also presents the results regarding urgent hospitalizations and all-cause death at 6 months of follow-up. During the study period, the number of hospitalizations was very few, and there were no deaths in any of the study arms. In this context, no statistically significant differences between the two study arms were identified.

Discussion

In this pilot, randomized, controlled trial conducted in a single center in which a comprehensive CRP was in place, a nurse-led intervention including follow-up, serial lipid level controls, and subsequent optimization of lipid-lowering therapy if appropriate was associated with an improved management of LDL cholesterol levels compared to standard of care alone. Also, the intervention was associated with improved blood pressure control among individuals with a diagnosis of hypertension. If replicated in larger studies, the present findings may have important implications for the chronic management of patients with IHD, in many of whom the treatment goals recommended by clinical practice guidelines are currently not achieved.

In our study, despite being included in a comprehensive, multidisciplinary CRP, only 37% of the individuals in the standard care arm achieved the LDL target of ≤70mg/dL 6 months after discharge. This observation, which is consistent with the poor results published in the

literature,[7,8] highlights the need for additional efforts aimed at improving adherence to and treatment titration of lipid-lowering medications in patients with IHD. Of note, despite the additional interventions included in the intervention arm, 38% of participants in this group still did not achieve the LDL ≤70mg/dL target, which stresses the complexity of the issue and the difficulty to achieve a full success in this patient population.

Our results are consistent with those from prior studies assessing the efficacy of nurse-led cardiovascular risk reduction programs in patients with IHD. In the Randomised Evaluation of Secondary Prevention by Outpatient Nurse SpEcialists (RESPONSE) trial,[20,21] which included 754 patients from The Netherlands admitted for an acute coronary syndrome and exposed to a nurse-coordinated secondary prevention intervention (comprising 4 outpatient clinic visits to a cardiovascular nurse focused on healthy lifestyle recommendations, improvement of biometric risk factors and of medication adherence, and in which medication adjustment was conducted when necessary), there was a significant improvement in overall cardiovascular risk factor control, in 10-year estimated CVD death risk after 12 months, and in re-hospitalizations among individuals exposed to the intervention as compared to those in the standard care arm. Specifically regarding LDL cholesterol, although study nurses had been trained and were highly confident about their ability to achieve drug-related treatment targets,[22] differences between the 2 study arms were smaller than in our study, with a target of LDL cholesterol <2.5mmol/L (≈100mg/dL) being achieved in 80% of patients in the intervention arm compared to 69% in the standard care arm (as compared to 97% and 67%, respectively, in our study). Our results are also consistent with those from observational studies evaluating similar nurse-led programs,[23,24] as well as with experimental evaluations conducted in other groups of cardiovascular patients.[16] In this context, to our knowledge our analysis is the first to assess the efficacy of a nurse-based

intervention in terms of achieving the LDL target recommended in the 2016 ESC guidelines,[7] as well as in terms of achieving the LDL reduction recommended in the 2013 American College of Cardiology / American Heart Association (ACC/AHA) cholesterol treatment guidelines.[25]

Our findings have important clinical implications. The intervention, which could be easily incorporated to a standard CRP, resulted not only in clear benefits in terms of lipid level management, but also in improved management of blood pressure levels among individuals with hypertension. Because the intervention did not include any actions aimed at modifying the patient's blood pressure lowering pharmacologic treatment, the latter was likely the consequence of the increased contact between the healthcare personnel and patients leading to greater adherence to healthy lifestyle recommendations. Our study identifies thus an invaluable opportunity to improve the secondary prevention management of patients with IHD.

Study limitations

Some study limitations must be acknowledged. First, patients were recruited from a single medical center, therefore, generalizability of our findings to other patient populations and healthcare environments may be limited. Nevertheless, the benefits of closer follow-up observed in our study are likely to apply to other environments. Second, the small sample size may have impacted statistical power and our ability to identify statistically significant differences between the groups. This, however, did not prevent us from observing significant differences between the study arms in several endpoints, including the pre-specified primary study endpoint, which supports the efficacy of the intervention. On the other hand, our analysis was clearly underpowered to identify differences in clinical events, or in other study endpoints such as differences in tobacco use during follow-up.

Third, the small sample size also prevented conducting detailed evaluations of different lipid-lowering pharmacologic management strategies. For the same reason, subgroup analyses in clinically relevant subgroups of patients were not feasible either. Finally, because the study was conducted before 2015, this prevented gaining insights on the effectiveness specifically of PCSK9 inhibitors[26] in patients with IHD. These limitations stress the pilot nature of the present analysis, and the need to replicate our findings in larger, multi-center, contemporary cohorts.

Conclusions

In this small experimental study, a nurse-led intervention added to a standard CRP including follow-up, serial lipid level checks, and subsequent optimization of lipid-lowering therapy, was associated with a markedly improved management of LDL cholesterol levels compared to a standard CRP program alone. Our findings highlight the opportunity that nurse-led post-discharge follow-up aggressive lipid-lowering interventions represent for the optimization of risk factor control, specifically of LDL cholesterol in patients with IHD.

Implications for practice

1. Strategies are needed to optimize secondary prevention in post-MI patients
2. A nurse-led intervention improved LDL cholesterol control at 6 months
3. Other risk factor-control benefits were also observed at 6 months
4. Easily incorporable to a standard rehabilitation program

Conflicts of Interest

The authors have no conflicts of interest relevant to the content of this manuscript.

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Author Contributions

All authors have contributed to and approved the content of this manuscript.

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FIGURE LEGENDS

Figure 1. Flow of the study participants.

This flowchart displays the flow of the participants included in the study. There were no losses to follow-up or study arm crossovers during the 6-month study follow-up.

Abbreviations: N = number

Figure 2A. Absolute atorvastatin dose change at 6 months in milligrams per day, by study arm.

Y axis: number of patients.

Figure 2B. Absolute LDL cholesterol change at 6 months in, mg/dL, by study arm.

Y axis: number of patients.

TABLES

Table 1. Baseline characteristics of the study participants.

	Overall (N = 78)	Standard Care (N = 39)	Intervention (N = 39)	P Value
Sociodemographic characteristics and cardiovascular risk factors				
Age, years	61 (54, 7)	60 (53, 7)	62 (55, 7)	0.382
Male sex	65 (83.3)	33 (84.6)	32 (82.1)	0.761
Active smoker	18 (23.1)	8 (20.5)	10 (25.6)	0.591
Diabetes mellitus	24 (30.8)	9 (23.1)	15 (38.5)	0.141
Hypertension	59 (75.6)	27 (69.2)	32 (82.1)	0.187
Dyslipidemia	51 (65.4)	25 (64.1)	26 (66.7)	0.812
Clinical variables at discharge				
Systolic blood pressure, mmHg	116 (108, 129)	115 (107, 128)	118 (109, 137)	0.385
Diastolic blood pressure, mmHg	71 (64, 7)	71 (64, 8)	70 (62, 7)	0.418
LVEF, %	60 (55, 6)	60 (49, 6)	60 (53, 6)	0.572
Reason for hospitalisation				
STEMI	35 (44.9)	19 (48.7)	16 (41)	0.679*
NSTEMI	30 (38.5)	13 (33.3)	17 (43.6)	
Unstable angina	12 (15.4)	6 (15.4)	6 (15.4)	
Stable angina	1 (1.3)	1 (2.6)	0 (0)	
Laboratory test results at admission				
Glucose, mg/dL	109 (98, 127)	109 (98, 136)	108 (98, 123)	0.642
Creatinine, mg/dL	0.80 (0.70, 1.00)	0.80 (0.70, 1.00)	0.90 (0.80, 1.00)	0.223
Urea, mg/dL	38 (28, 47)	34 (26, 45)	41 (30, 49)	0.053
Haemoglobin, g/dL	14.1 (13.2, 15.1)	14.2 (13.3, 15.1)	14.0 (12.8, 15.1)	0.549
HbA1c, %	5.8 (5.5, 6.6)	5.7 (5.4, 6.3)	6.1 (5.5, 7.0)	0.084
Total cholesterol, mg/dL	176 (150, 215)	178 (162, 216)	166 (136, 214)	0.393
LDL cholesterol, mg/dL	103 (84, 142)	103 (93, 140)	103 (79, 142)	0.566
HDL cholesterol, mg/dL	41 (32, 49)	44 (33, 55)	40 (28, 48)	0.193
Triglycerides, mg/dL	124 (99, 179)	119 (98, 179)	130 (104, 174)	0.693
Lipid-lowering medication use at				

discharge				
Statin use at discharge	77 (98.7)	38 (97.4)	39 (100)	1.000*
Atorvastatin	65 (83.3)	31 (81.6)	34 (87.2)	0.755*
Simvastatin	2 (2.6)	1 (2.6)	1 (2.6)	
Rosuvastatin	10 (12.8)	6 (15.8)	4 (10.3)	
Equivalent daily dose of atorvastatin	40 (40, 40)	40 (40, 40)	40 (40, 40)	0.877

Data presented as median (interquartile range) or n (%). Percentages may not sum 100% due to rounding
*P value calculated using Fisher's exact test
Abbreviations: HbA1c = glycosilated haemoglobin; HDL = high density lipoprotein; LDL = low density lipoprotein; LVEF = left ventricle ejection fraction; NSTEMI = non-ST elevation myocardial infarction; STEMI = ST elevation myocardial infarction

Table 2. Lipid-lowering medication use and serum lipid levels at 6 months of follow-up.

	Standard Care (N = 39)	Intervention (N = 39)	P Value
Lipid-lowering medication use			
Any statin, %	37 (94.9)	39 (100.0)	0.494*
Ezetimibe, %	1 (2.6)	11 (28.2)	0.003*
Lipid-lowering medication changed, %	8 (20.5)	19 (48.7)	0.009
Equivalent daily dose of atorvastatin, mg	40 (40, 40)	40 (40, 80)	0.045
Absolute change in daily dose of atorvastatin, mg	0 (0, 0)	0 (0, +40)	0.036
Relative change in daily dose of atorvastatin, %	0 (0, 0)	0 (0, +100)	0.036
Laboratory test results			
Total cholesterol, mg/dL	151 (129, 176)	130 (115, 147)	<0.001
Absolute change in total cholesterol, mg/dL	-45 (-63, -3)	-43 (-70, -14)	0.635
Relative change in total cholesterol, %	-24 (-33, -1)	-25 (-37, -9)	0.389
LDL cholesterol, mg/dL	82 (63, 108)	67 (60, 78)	0.006
Absolute change in LDL cholesterol, mg/dL	-35 (-42, +4)	-34 (-69, -16)	0.062
Relative change in LDL cholesterol, %	-26 (-38, +5)	-36 (-54, -19)	0.025
HDL cholesterol, mg/dL	48 (41, 55)	43 (37, 50)	0.051
Absolute change in HDL cholesterol, mg/dL	+6 (-6, +11)	+5 (-4, +9)	0.581
Relative change in HDL cholesterol, %	+13 (-11, +30)	+11 (-8, +33)	0.964
Triglycerides, mg/dL	99 (77, 132)	95 (69, 114)	0.246
Absolute change in triglycerides, mg/dL	-41 (-60, +13)	-30 (-88, -6)	0.995
Relative change in triglycerides, mg/dL	-28 (-43, +18)	-27 (-51, -5)	0.686
LDL cholesterol clinical management endpoints			
LDL cholesterol ≤100 mg/dL	18 (66.7)	36 (97.3)	0.001*
LDL cholesterol ≤70 mg/dL	10 (37.0)	23 (62.2)	0.047
LDL reduction at 6months ≥50%	1 (2.6)	10 (25.6)	0.007*

Data presented as median (interquartile range) or n (%). Percentages may not sum 100% due to rounding
*P value calculated using Fisher's exact test
Abbreviations: HDL = high density lipoprotein; LDL = low density lipoprotein

Table 3. Management of other cardiovascular risk factors, and clinical events at 6 months of follow-up.

	Standard Care (N = 39)	Intervention (N = 39)	P Value
Management of other cardiovascular risk factors at 6 months			
Systolic blood pressure, mmHg	130 (120, 140)	126 (119, 134)	0.270
Diastolic blood pressure, mmHg	76 (66, 82)	72 (62, 79)	0.038
SBP <140 and DBP <90 mmHg	26 (66.7)	33 (84.6)	0.065
Change in blood pressure-lowering medication	0 (0)	5 (12.8)	0.055*
HbA1c, %	5.8 (5.5, 6.3)	6.1 (5.9, 6.4)	0.123
Active smoker	4 (10.3)	3 (7.7)	1.000*
Management of blood pressure in individuals with hypertension (n=59)			
Systolic blood pressure, mmHg	132 (123, 144)	127 (120, 135)	0.114
Diastolic blood pressure, mmHg	76 (66, 85)	72 (64, 76)	0.044
SBP <140 and DBP <90 mmHg	17 (63.0)	28 (87.5)	0.035*
Change in blood pressure-lowering medication	0 (0.0)	4 (12.5)	0.118*
Management of HbA1c in individuals with diabetes (n=24)			
HbA1c, %	6.2 (5.8, 7.3)	6.4 (6.0, 7.2)	0.380
HbA1c <7.0%	5 (71.4)	7 (70.0)	1.000*
Clinical events during follow-up			
Urgent hospitalization	4 (10.3)	0 (0.0)	0.115*
All-cause death	0 (0.0)	0 (0.0)	-

Data presented as median (interquartile range) or n (%)
*P value calculated using Fisher's exact test
Abbreviations: HbA1c = glycosilated haemoglobin; DBP = diastolic blood pressure; SBP = systolic blood pressure

FIGURES

Figure 1. Flow of the study participants.

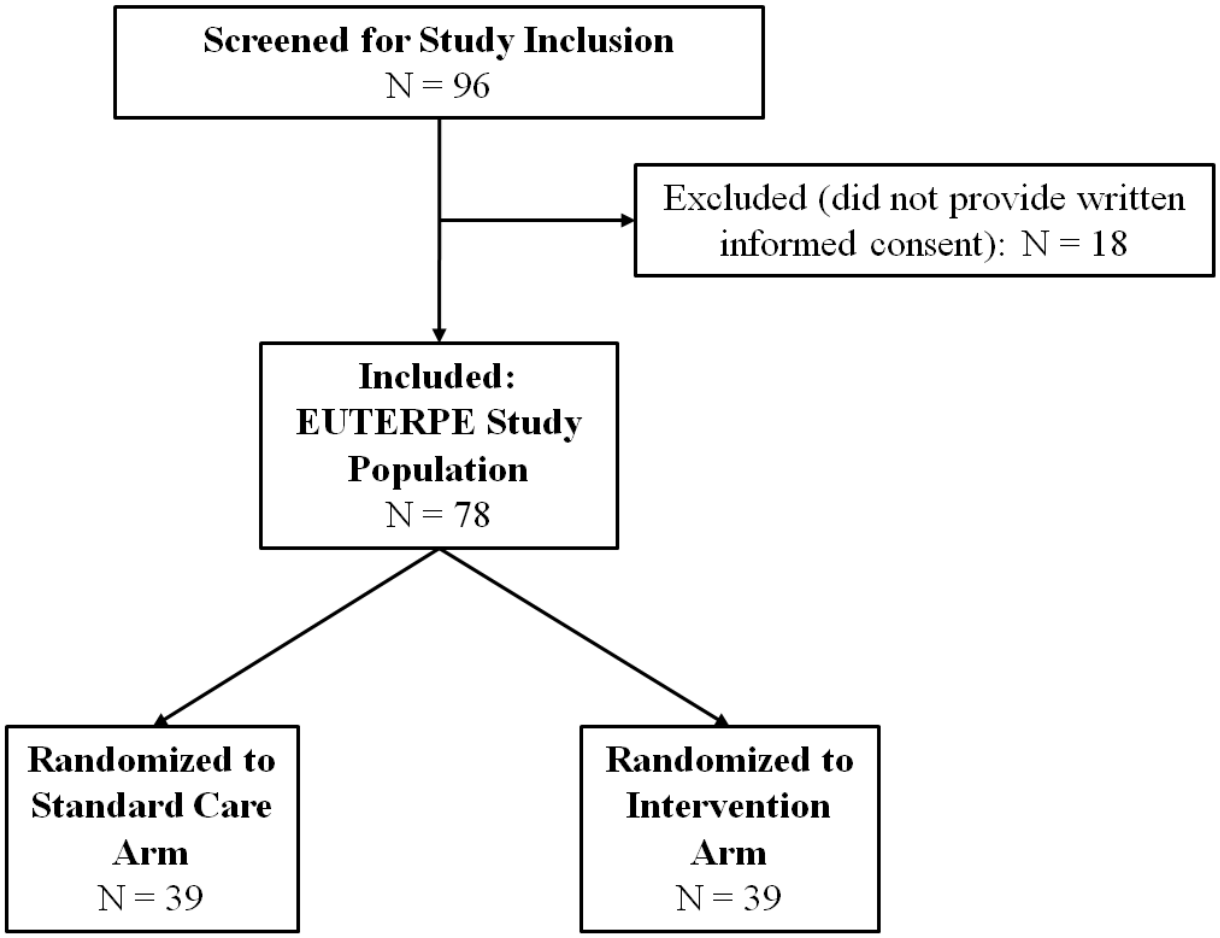


Figure 2A. Absolute atorvastatin dose change at 6 months in milligrams per day, by study arm.

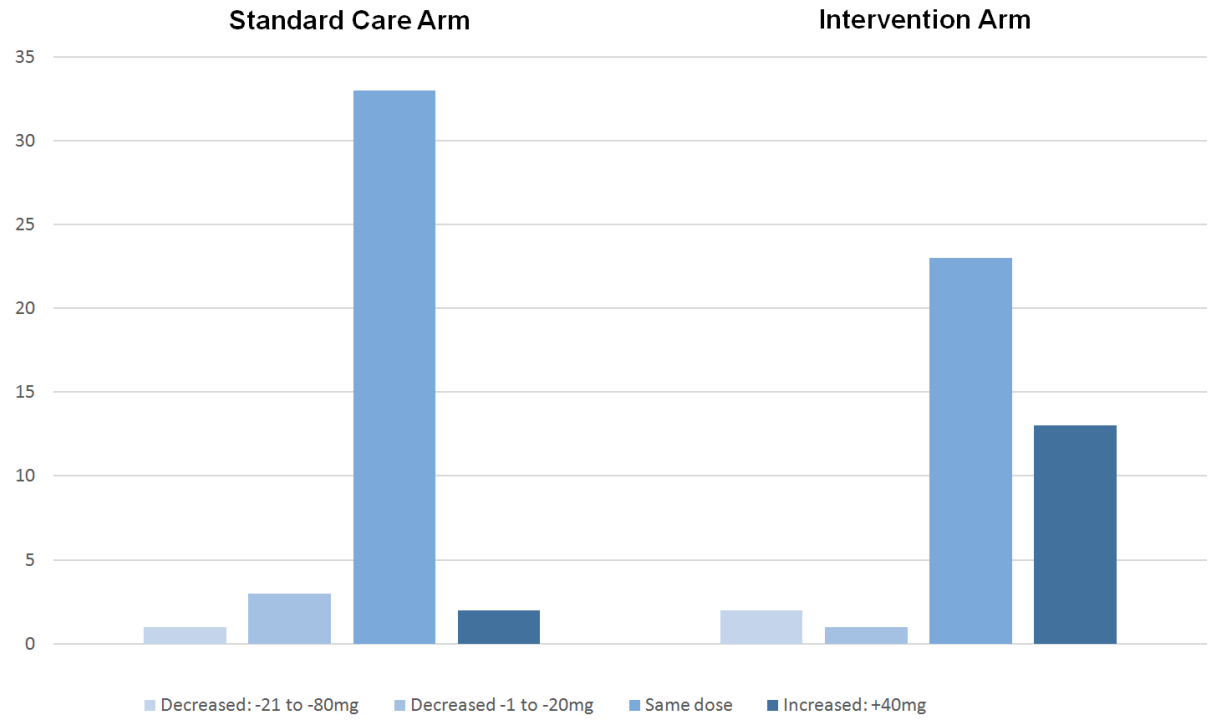
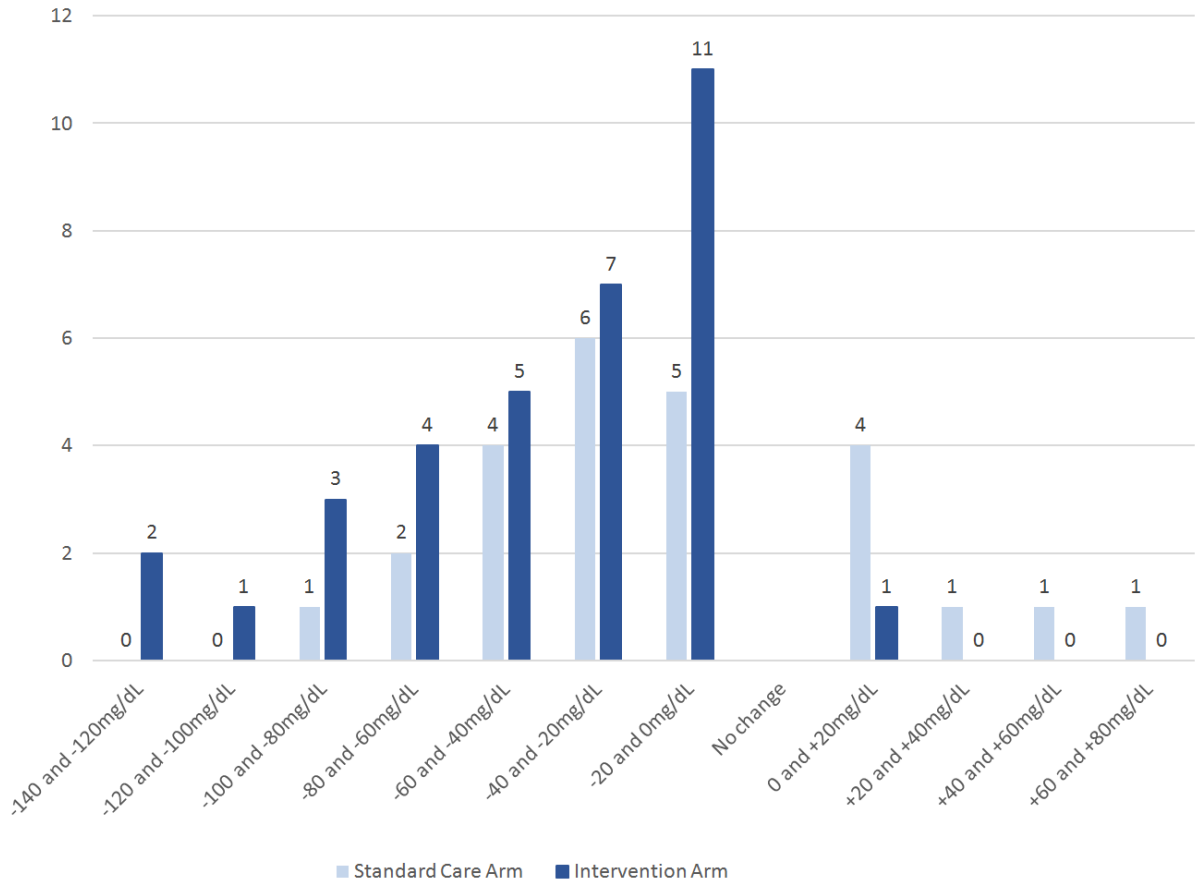
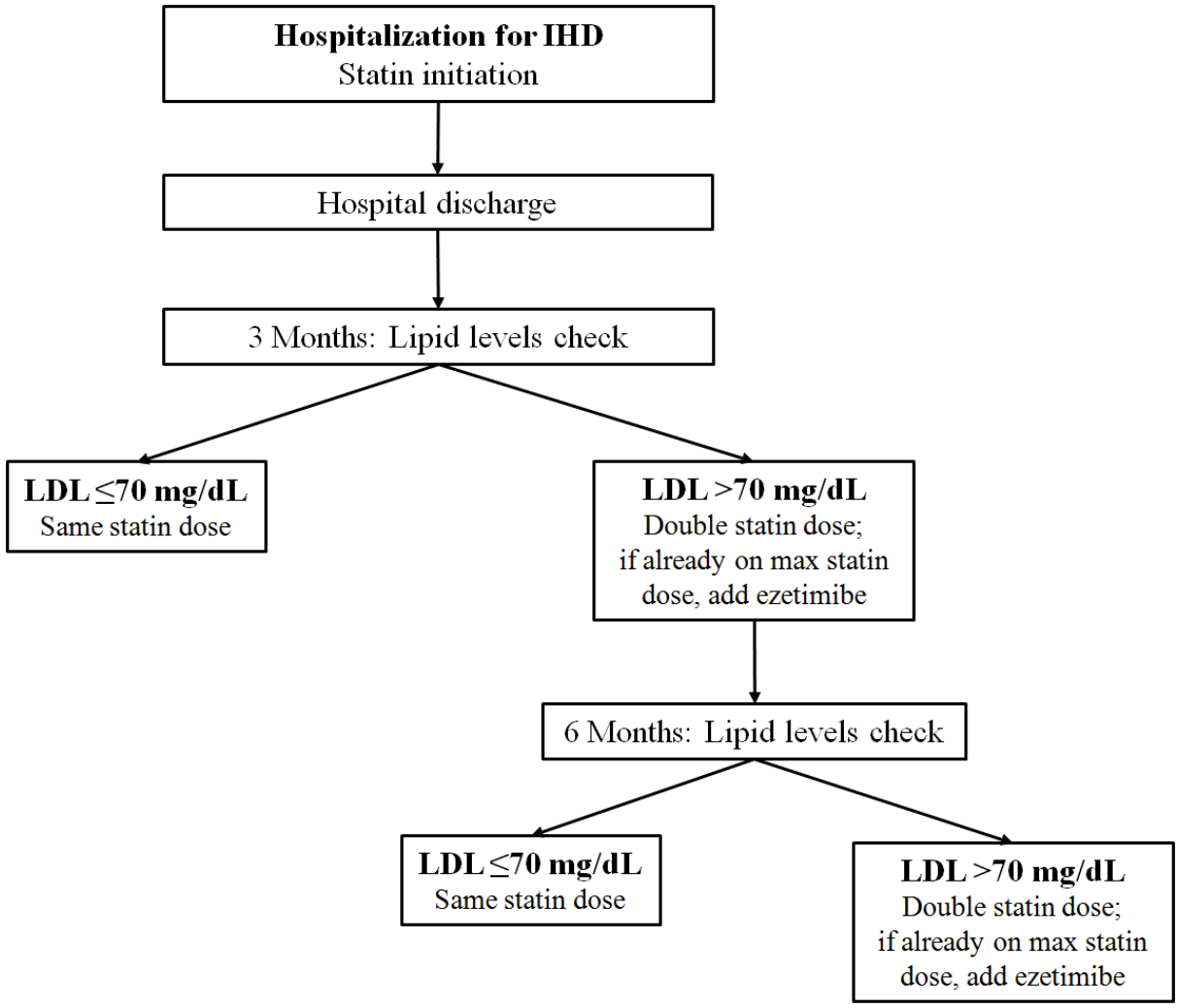


Figure 2B. Absolute LDL cholesterol change at 6 months in, mg/dL, by study arm.



SUPPLEMENTARY FIGURES

Figure S1. Lipid-lowering pharmacological algorithm in the intervention arm.



Abbreviations: IHD = ischaemic heart disease; LDL = low density lipoprotein