ESC European Heart Journal - Quality of Care and Clinical Outcomes (2026) **00**, 1–12
https://doi.org/10.1093/ehjqcco/qcag021

ORIGINAL ARTICLE

Sustainable and effective lipid-lowering management: prevention strategies from the BRING-UP prevention study

Furio Colivicchi[1], Pier Luigi Temporelli [2], Francesco Fattirolli[3], Maurizio Giuseppe Abrignani[4], Alessandro Alonzo[1], Marcello Arca[5], Maurizio Averna [6,7], Daniele Bertoli[8], Paolo Calabrò [9], Leonardo Calò [10], Stefano Carugo[11], Alberico Luigi Catapano[12,13], Martina Ceseri[14], Stefania Angela Di Fusco[1], Andrea Di Lenarda [15], Gianna Fabbri[14], Michele Massimo Gulizia[16], Giuseppe La Rosa[17], Donata Lucci[14], Simone Maffei[18], Alessandro Navazio [19], Fabrizio Oliva [20], Francesco Orso[14], Carmine Riccio[21], Nicola Scelza[22], Domenico Gabrielli [14,23], and Aldo Pietro Maggioni [14,*], on the behalf of BRING-UP Prevention[†]

[1]Clinical and Rehabilitation Cardiology Department, San Filippo Neri Hospital, ASL Roma 1, 00135 Roma, Italy; [2]Division of Cardiac Rehabilitation, Istituti Clinici Scientifici Maugeri, IRCCS, 28013 Gattico-Veruno, Italy; [3]Department of Experimental and Clinical Medicine, Careggi University Hospital, University of Florence, 50134 Firenze, Italy; [4]Cardiology-ICCU, P. Borsellino Hospital, ASP Trapani, 91025 Marsala, Italy; [5]Department of Translational and Precision Medicine (DTPM), Sapienza University of Rome, Policlinico Umberto I, 00161 Rome, Italy; [6]Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties (PROMISE), University of Palermo, 90127 Palermo, Italy; [7]Istituto di Biofisica, CNR, 90146 Palermo, Italy; [8]Rehabilitation Cardiology Department, Ospedale San Bartolomeo, 19038 Sarzana, Italy; [9]Division of Cardiology, A.O.R.N. 'Sant'Anna e San Sebastiano', 81100 Caserta, Italy; [10]Cardiology Unit, Policlinico Casilino, 00169 Rome, Italy; [11]Department of Cardio-Thoracic-Vascular Diseases, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, 20122 Milan, Italy; [12]Department of Pharmacological and Biomolecular Sciences, University of Milan, 20133 Milano, Italy; [13]Center for the Study of Atherosclerosis, IRCCS Multimedica, 20100 Milano, Italy; [14]ANMCO Research Centre, Heart Care Foundation, Firenze, 50121 Florence, Italy; [15]Cardiovascular Centre, University Hospital and Health Services of Trieste, 340125 Trieste, Italy; [16]Cardiology Division, Garibaldi-Nesima Hospital, 95122 Catania, Italy; [17]Cardiology, Santa Barbara Hospital, 93012 Gela, Italy; [18]Cardiology Unit, Presidio Ospedaliero San Salvatore, AST PU, 61121 Pesaro, Italy; [19]Cardiology Department, P.O. Santa Maria Nuova, Azienda USL di Reggio Emilia-IRCCS, 42100 Reggio Emilia, Italy; [20]Cardiology Unit, Niguarda Hospital, 20162 Milano, Italy; [21]Cardiovascular Department, Sant'Anna e San Sebastiano Hospital, 81100 Caserta, Italy; [22]Cardiology Rehabilitation, Auxilium Vitae Volterra, 56048 Volterra, Italy; and [23]Department of Cardio-Thoracic and Vascular Medicine and Surgery, Division of Cardiology, A.O. San Camillo-Forlanini, 00152 Roma, Italy

Received 27 August 2025; revised 4 November 2025; accepted 3 February 2026; online publish-ahead-of-print 8 February 2026

Aims

Adherence to guideline recommendations for secondary prevention appears to be inadequate, even in cardiology centres. To narrow the gap between guideline recommendations and what is implemented in clinical practice, we designed the BRING-UP Prevention project.

Methods and results

BRING-UP Prevention is a nationwide, observational, prospective, multicenter study enrolling patients with a prior atherothrombotic event. The study consists of two 3-month enrolment phases followed by a 6-month follow-up, with each phase preceded by an educational intervention. Data presented here mainly focus on the percentage of patients at goal for LDL-cholesterol (LDL-C) (<55 mg/dL) at the 6-month follow-up in the recently completed first enrolment phase. Secondary endpoints are blood pressure, glycaemic and weight control, and smoking cessation. Over 3 months, 189 cardiology centres recruited 4790 patients. Follow-up data at 6 months were available for 4643 patients (97%) and LDL-C was available for 4334 of them. The rate of patients with

*Corresponding author. Tel: + 39 055 5101361, Email: maggioni@heartcarefoundation.it
[†]See Appendix in the Supplemental Material for a complete list of Steering Committee members, Coordinating Centre and List of Collaborators by Site.

LDL-C < 55 mg/dL increased from 33% to 58.1%, with absolute and relative increases of 25.1% and 76.1%, respectively. At 6 months, 94.9% of patients were prescribed statins. Atorvastatin and rosuvastatin were the most prescribed statins, mostly at high doses. Ezetimibe was prescribed in 84% of cases. PCSK9i monoclonal antibodies and inclisiran were prescribed in 8.3% of patients.

Conclusion BRING-UP prevention achieved its primary goal to increase the percentage of patients at the LDL-C goal, demonstrating that, in many patients, this goal can be achieved by increasing the use of low-cost therapies.

ClinicalTrial.gov NCT06275113

Lay summary Many people who have already had heart problems do not fully follow medical guidelines to prevent another event. In particular, their levels of 'bad' cholesterol (LDL-C) often remain too high. To help close the gap between what the guidelines recommend and what actually happens in everyday care, we created a project called BRING-UP Prevention. This project focused on educating doctors and collecting information about their patients.

After the programme:

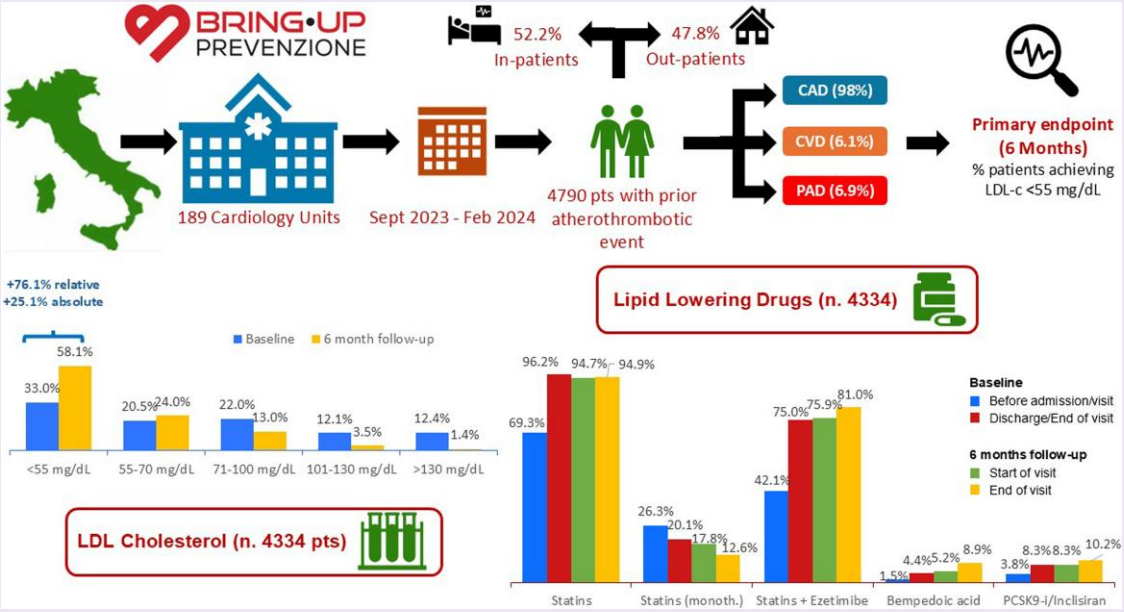
The number of patients who reached their target LDL-C level went up from 33% to 58%.

This improvement was achieved mostly with standard, affordable medications, such as statins, often combined with ezetimibe.

We also saw small improvements in blood pressure control and smoking cessation. However, blood sugar levels and weight management still need more attention in the future.

Our results show that studies aimed at helping doctors follow prevention guidelines more closely can quickly lead to better cholesterol control. This is especially true when many cardiology centres—of all sizes and technological levels—take part in the initiative, as they did in the BRING-UP Prevention project across Italy.

Graphical abstract



Keywords Secondary prevention • LDL-cholesterol • Guideline • Implementation science • Hypolipidemic agents

Key Learning Points

What is already known

- Secondary prevention strategies, if appropriately implemented, can reduce the recurrence of cardiovascular events.
- Claims data and cardiology registries show that the use and adherence to these strategies are suboptimal and the rate of patients at goal according to guidelines is far from satisfactory.

What this study adds

- The active involvement of a very large community of cardiology units of a whole country in an *ad hoc* programme of guidelines implementation and guided data collection can substantially improve the rate of patients at goal for LDL-C.
- The improvement can be obtained in most patients with the use of low-cost therapies such as high-dose statins, in most cases in association with ezetimibe.
- More efforts should be made in the future to control HbA1c in diabetics and body weight.

Introduction

Cardiovascular disease (CVD) is currently the leading cause of death worldwide, with 20.5 million people dying from CVD each year, accounting for nearly one-third of all deaths worldwide.[1] Most of the CVD burden is due to atherosclerotic CVD, which is the leading cause of premature death, disability, and healthcare costs worldwide.[2-5]

The primary goals of secondary prevention are to improve survival, enhance quality of life, and prevent recurrent cardiovascular events by addressing modifiable risk factors, optimizing pharmacological therapies, and promoting lifestyle changes.[6,7] Secondary prevention strategies typically involve a multifactorial approach, including the use of antiplatelet agents, lipid-lowering agents, blood pressure (BP) control, and diabetes management.[8] In addition, lifestyle interventions such as smoking cessation, physical activity, and dietary modification play a critical role in reducing cardiovascular risk.[9] Despite the established benefits of these interventions, there are large gaps between guidelines and practice in the prevention and treatment of CVD.[10,11] The residual risk of recurrent events remains high in all European countries.[12] In Italy, all treatments recommended by current guidelines[6,13,14] for the control of BP and the reduction of LDL and non-HDL cholesterol, such as statins, ezetimibe, bempedoic acid, proprotein convertase subtilisin/kexin type 9 inhibitors (PCSK9i) monoclonal antibodies, and inclisiran (for patients not achieving goal despite statin and/or ezetimibe), are available and reimbursed by the National Health Service (NHS). Despite this favourable regulatory environment, administrative data and cardiology registries show that the use and adherence to these recommended treatments in Italy is suboptimal and the rate of patients at goal according to guidelines is far from satisfactory, ranging from 30% to 40% of patients exposed to a secondary prevention strategy.[15-17]

Previous evidence has shown that an implementation strategy based on physician education, training, tutoring of taking care physicians, and guided data collection can play an important role in increasing awareness and adherence to guidelines.[18-20] The BRING-UP Prevention project combined physician education and guided patient data collection to reduce the gap between guideline recommendations and real-world cardiology practice.[21]

Methods

BRING-UP Prevention study was performed in a large number of Italian cardiology centres well representing the Italian cardiology reality in terms of geographical distribution and level of hospital facilities (see Supplementary material online, *Figure S1*). The study was prospective, multicenter, and designed in two phases, each consisting of an educational intervention followed by a 3-month data collection phase (see Supplementary material online, *Figure S2*). We invited to participate in the study 611 sites of the Italian Association of Hospital Cardiologists (ANMCO) with availability of beds or with a rehabilitation centre or a dedicated clinic for secondary prevention. Of the 224 sites that expressed their interest, 199 were activated, and 189 enrolled at least one patient. Thirty-one percent of the participating sites had a structured secondary prevention clinic or a rehabilitation centre.

During the first educational intervention, international guidelines on secondary prevention were presented and discussed, along with other topics considered relevant to the management of secondary prevention. The educational programme was extended to a very large number of cardiologists from the participating centres. Overall, 178 Investigators participated from 72% of sites. Members of the Steering committee, recognized expert leaders in the field of secondary prevention in Italy, performed interactive presentations on the following topics: secondary prevention real world data and cardiology registries, guideline recommendations, obstacles and possible strategies for guidelines implementation, residual risk (hypertriglyceridaemia, Lp(a), management of obesity, inflammation), the role of comorbidities [i.e. diabetes, chronic kidney disease (CKD)] and lifestyle modifications. All presentations were pre-recorded and were immediately available for investigators on the study website. Investigators who did not attend the investigator meetings were required to do a self-training with the online materials. Self-training completion was mandatory to receive the credentials to access the electronic case report form (eCRF) platform (see Supplementary material online, *Table S1*).

The baseline characteristics of patients enrolled in the BRING-UP Prevention were already published.[21]

All patients included in the study then entered a longitudinal follow-up of 6 months for primary and secondary endpoints evaluation and of 12 months for exploratory endpoint evaluation. This manuscript reports the results of the first 6 months of follow-up.

The study conforms to the principles outlined in the Declaration of Helsinki. The protocol has been approved by each local ethics committee in accordance with the national regulations. Each patient provided written informed consent to participate in the study.

Study population

All centres were asked to enrol patients for 3 months at the time of discharge (after regular hospitalization or day hospitalization) or during an outpatient visit in patients with a documented prior atherothrombotic event. These events were categorized as following: coronary artery disease (CAD) defined as prior acute coronary syndrome (ACS), prior coronary artery bypass grafting (CABG), prior percutaneous coronary intervention (PCI); cerebrovascular disease (CBVD) defined as ischaemic stroke, prior carotid vascular intervention; peripheral artery disease

(PAD) defined as prior peripheral bypass surgery or angioplasty, limb or foot amputation, intermittent claudication with objective evidence of PAD, ankle-brachial index (ABI) < 0.9.

Patients with very severe disease affecting short to medium term life expectancy or participating in interventional studies were excluded.

Also, no specific protocols or recommendations for evaluation, management, and/or treatment were provided during this observational study. However, a strong recommendation to follow the guidelines valid for the period of patients' enrolment[7,22] was provided to all participant cardiologists during the educational programme.

Data collection

Data collection was characterized by reminders that appeared in the eCRF when a guideline-recommended treatment or target was not prescribed or not achieved. Cardiologists were free to decide what to do, but in the case of non-prescription, when treatment was theoretically indicated, they had to report the reason for their decision in the eCRF. Data were collected using an *ad hoc* web-based system. Variables collected include demographic characteristics, clinical characteristics, medical history, laboratory tests, diagnostic procedures, pharmacologic and non-pharmacologic treatments, survival status, causes of death, and need for hospitalization or rehospitalization and related causes at 6 and 12 months.

End points

The primary end point of this study was the rate of patients at goal for LDL cholesterol (LDL-C) (<55 mg/dL) at 6 months.

The secondary endpoints at 6 months were:

- Rate of patients at goal for office BP measure [systolic blood pressure (SBP)/diastolic blood pressure (DBP) < 130/80 mmHg);
- Rate of diabetic patients at goal for HbA1c (<7%);
- Rate of patients with a body mass index (BMI) > 27 kg/m^2 who show a weight loss of at least 10%;
- Level of adherence to the recommendations for lifestyle modifications (smoking, diet, exercise);
- Level of adherence to the guidelines recommended pharmacological treatments.

Exploratory endpoints were the rates of occurrence of clinical events (all-cause death, recurrent atherothrombotic events, all-cause hospitalization, specific causes of death and hospitalization) during the 12 months follow-up.

Data were also collected on the group of patients not treated with statins or treated with low-dose statins to assess the prevalence of total or partial statin intolerance and to describe the characteristics and lipid-lowering treatments of this group of patients.

The data presented in this paper relate to the first 6-month follow-up and mainly address the primary endpoint of the study (including lipid-lowering treatments prescribed in these patients) with an overview of secondary endpoints achievement.

Statistical analysis and sample size calculation

The hypothesis was to improve adherence to the guidelines by 50% (an absolute 20% increase), aiming for 60% of patients to reach the LDL-C goal by the 6-month follow-up period. Assuming the recruitment of 1000 patients, the estimate of 60% of patients reaching the goal will have a 95% confidence interval of 57–63%.

In order to further improve the reliability of the estimate and to provide also reliable information in subgroups of patients with different prior atherothrombotic events and relevant comorbidities (specifically age, sex, diabetes mellitus, and CKD), we planned to enrol at least the total number of 3000 patients per enrolment phase.

Categorical variables are presented as percentages or number and percentages and compared using the chi-square test. Continuous variables are reported as means and standard deviations (SD), or as median and inter-quartile range (IQR), and compared using the *t*-test if normally distributed, and the Mann–Whitney *U* test, if not. We compared the baseline clinical characteristics, laboratory tests, and lipid-lowering medications prescribed at the enrolment visit of patients who did or did not achieve the LDL-C goal (<55 mg/dL) at 6 months. Multivariable logistic regression analysis was performed to identify covariates independently associated with failure to achieve LDL-C goal (<55 mg/dL) at 6 months, taking into account variables that were statistically significant at univariate analysis ($P < 0.05$). A *P*-value of less than 0.05 was considered statistically significant. All tests were two-sided. The analyses were performed using SAS software, version 9.4.

Results

From 15 September 2023 to 29 February 2024, 4790 patients were enrolled (mean age of 67 ± 11 years, 20% women); 2500 were discharged from the hospital, 2216 were treated as outpatients, and 74 were treated in the day hospital setting. Of the 4790 patients, 98% had CAD, 6.1% had CVD, and 6.9% had PAD. Each patient could have more than one inclusion criterion and, therefore, more than one vascular district involved.

At 6-month follow-up, data regarding vital status were available for 4643 patients (97%), while clinical data were available for 4510 (94.2%). The majority of these patients were followed in person at outpatient clinics. A flow-chart regarding follow-up procedures is provided in Supplementary material online, *Figure S3*. LDL-C was not available for 176 out of 4510 patients (4%) with follow-up performed as a clinic visit or a phone contact. Therefore, our final study population is composed of 4334 patients with a measure of LDL-C available at 6 months.

Table 1 shows the baseline characteristics of the population of 4334 patients, overall and according to attainment of the LDL-C goal. In brief, the goal was more frequently achieved in younger and male patients, in those with diabetes, in those with lower total and LDL-C at baseline, and in those receiving more intensive lipid-lowering treatment. Depression was more frequently associated with non-attainment of the LDL-C goal.

Atorvastatin or rosuvastatin was prescribed at discharge/end of visit in 93.8% of patients. High doses (40/80 mg atorvastatin and 20/40 mg rosuvastatin) were prescribed to 78.5% of patients, 73.3% of patients received high-intensity statins in combination with ezetimibe. From baseline to 6-month follow-up visit, we observed an increase of prescription and doses of statins and an increase in the association of statin plus ezetimibe (*Table 2*, *Figure 1*).

The proportion of patients with LDL-C < 55 mg/dL increased from 33% at baseline to 58.1% at 6 months, with absolute and relative increases of 25.1% and 76.1%, respectively (*Figure 2*). The increase in the percentage of patients achieving the goal was greater in those enrolled as inpatients than in outpatients (from 24.1% to 57.6% and 42.1% to 58.6%, respectively) (see Supplementary material online, *Figure S4*). Moreover, 24.2% of patients experienced a ≥ 50% reduction in LDL-C from baseline, while 19.9% reached both targets (LDL-C < 55 mg/dL and ≥50% LDL-C reduction from baseline), and 62.3% at least one of them.

Overall, the proportion of patients with LDL-C ≤ 70 mg/dL increased from 53.5% to 82.1%. At enrolment 69.3% of patients were receiving statins; this proportion increased to 96.2% at discharge/end of the outpatient visit. At the 6-month follow-up, 94.9% of patients remained on statin therapy.

Among the other lipid-lowering agents, ezetimibe was the most commonly prescribed drug both at baseline and at 6 months. At 6 months, prescriptions of PCSK9i monoclonal antibodies, inclisiran, and bempedoic acid had also increased, with overall use of these drugs increasing from 12.3% to 18.3%, (*Table 2*).

Table 1 Baseline characteristics of the total population of patients and by LDL-cholesterol goal achieved at 6-month follow-up

	Total population *n.* 4334	6-months LDL-C < 55 mg/dL *n.* 2518	6-months LDL-C ≥ 55 mg/dL *n.* 1816	*P*
Inclusion criteria				
CAD, *n.* (%)	4250 (98.1)	2484 (98.7)	1766 (97.3)	0.0009
CBVD, *n.* (%)	257 (5.9)	126 (5.0)	131 (7.2)	0.002
PAD, *n.* (%)	279 (6.4)	153 (6.1)	126 (6.9)	0.25
Ambulatory setting + DH, *n.* (%)	2138 (49.3)	1253 (49.8)	885 (48.7)	0.50
Age (years), mean ± SD	67 ± 11	67 ± 11	68 ± 11	0.007
Females, *n.* (%)	863 (19.9)	430 (17.1)	433 (23.8)	<0.0001
SBP (mmHg), mean ± SD	127 ± 16	127 ± 17	127 ± 16	0.73
Heart rate (bpm), mean ± SD	67 ± 11	67 ± 11	68 ± 11	0.41
Current smokers, *n.* (%) (*n.* 4025)	891 (22.1)	500 (21.3)	391 (23.3)	0.14
Regular physical activity, *n.* (%)				0.12
No	1581 (36.5)	891 (35.4)	690 (38.0)	
Yes	2230 (51.4)	1329 (52.8)	901 (49.6)	
Unknown/uncertain	523 (12.1)	298 (11.8)	225 (12.4)	
BMI ≤27 kg/m^2, *n.* (%)	2484 (57.3)	1440 (57.2)	1044 (57.5)	0.84
BMI ≥30 kg/m^2, *n.* (%)	854 (19.7)	499 (19.8)	355 (19.6)	0.83
Diabetes, *n.* (%)	1171 (27.0)	767 (30.5)	404 (22.3)	<0.0001
Type 1	26 (2.2)	19 (2.5)	7 (1.7)	
Type 2	1104 (94.3)	725 (94.5)	379 (93.8)	0.32
Unknown	41 (3.5)	23 (3.0)	18 (4.5)	
Hypertension, *n.* (%)	3274 (75.5)	1893 (75.2)	1381 (76.1)	0.65
Hypercholesterolaemia, *n.* (%)	3393 (78.3)	1922 (76.3)	1471 (81.0)	0.0009
Heart failure, *n.* (%)	556 (12.8)	290 (11.5)	266 (14.7)	0.009
Atrial fibrillation/flutter, *n.* (%)	615 (14.2)	336 (13.3)	279 (15.4)	0.15
Chronic kidney disease, *n.* (%)	476 (11.0)	284 (11.3)	192 (10.6)	0.75
COPD, *n.* (%) (*n.* 4160)	367 (8.8)	204 (8.4)	163 (9.4)	0.30
Cancer, *n.* (%)	308 (7.1)	166 (6.6)	142 (7.8)	0.12
Depression, *n.* (%) (*n.* 4201)	198 (4.7)	98 (4.0)	100 (5.7)	0.009
Self-sufficient, *n.* (%)	3938 (90.9)	2271 (90.2)	1667 (91.8)	0.02
EF %, mean ± SD (*n.* 4142)	52.9 ± 9.4	53.0 ± 9.3	52.9 ± 9.6	0.66
Creatinine, mean ± SD (*n.* 4192)	1.1 ± 0.6	0.6 ± 0.8	0.7 ± 0.8	0.24
Tryglicerides, median [IQR] (*n.* 4332)	103 [79–138]	101 [77–137]	105 [81–138]	0.002
Total cholesterol at baseline, mean ± SD	142.6 ± 45.5	136.0 ± 45.6	151.8 ± 43.8	<0.0001
LDL cholesterol at study at baseline, mean ± SD	77.8 ± 41.0	71.9 ± 41.4	86.1 ± 38.9	<0.0001
Lipid-lowering drugs prescribed at baseline				
Number of lipid lowering drugs, *n.* (%)				<0.0001
0	29 (0.7)	6 (0.2)	23 (1.3)	
1	943 (21.8)	475 (18.9)	468 (25.8)	
2	2970 (68.5)	1786 (70.9)	1184 (65.2)	
>2	392 (9.0)	251 (10.0)	141 (7.7)	
Statins, *n.* (%)				<0.0001
No	167 (3.9)	72 (2.9)	95 (5.2)	
Statin low intensity	25 (0.6)	10 (0.4)	15 (0.8)	
Statin low intensity and ezetimibe	75 (1.7)	36 (1.4)	39 (2.2)	
Statin high intensity	890 (20.5)	464 (18.4)	426 (23.5)	
Statin high intensity and ezetimibe	3177 (73.3)	1936 (76.9)	1241 (68.3)	

Continued

Table 1 *Continued*

	Total population *n.* 4334	6-months LDL-C < 55 mg/dL *n.* 2518	6-months LDL-C ≥ 55 mg/dL *n.* 1816	*P*
Statins intolerance, *n.* (%)[a]				0.06
No	4130 (96.8)	2429 (97.3)	1701 (96.1)	
Partial	37 (0.9)	17 (0.7)	20 (1.1)	
Total	100 (2.3)	50 (2.0)	50 (2.8)	
PCSK9-i monoclonal antibodies or Inclisiran, *n* (%)	358 (8.3)	271 (10.8)	87 (4.8)	<0.0001

[a]Evaluated on 4267 patients with statins prescribed, or not prescribed due to intolerance.
In brackets, the number of patients with information available.
BMI, body mass index; CAD, coronary artery disease; CBVD, cerebrovascular disease; COPD, chronic obstructive pulmonary disease; DH, day hospital; EF, ejection fraction; IQR, inter-quartile range; LDL-C, low-density lipoprotein cholesterol; PAD, peripheral artery disease; PCSK9-i, proprotein convertase subtilisin/kexin type 9 inhibitors; SBP, systolic blood pressure; SD, standard deviation.

Table 2 **Lipid-lowering drugs at baseline and at 6-months follow-up (*n* = 4334)**

Drug	Baseline		6 months follow-up	
	Before admission/start of visit *n.* (%)	Discharge/end of visit *n.* (%)	Start of visit *n.* (%)	End of visit *n.* (%)
Statins	3004 (69.3)	4167 (96.2)	4106 (94.7)	4111 (94.4)
Statins + ezetimibe	1823 (42.1)	3252 (75.0)	3288 (75.9)	3511 (81.0)
Statins + other lipid lowering drug	1855 (42.8)	3297 (76.1)	3332 (76.9)	3565 (82.3)
At least one other lipid lowering drug associated or not with statins	2002 (46.2)	3437 (79.3)	3501 (80.8)	3754 (86.6)
Ezetimibe	1936 (44.7)	3351 (77.3)	3413 (78.8)	3653 (84.3)
Fibrates	38 (0.9)	32 (0.7)	26 (0.6)	32 (0.7)
Evolocumab	67 (1.6)	139 (3.2)	127 (2.9)	157 (3.6)
Alirocumab	75 (1.7)	153 (3.5)	151 (3.5)	184 (4.3)
Inclisiran	24 (0.6)	66 (1.5)	81 (1.9)	103 (2.4)
Bempedoic acid	65 (1.5)	190 (4.4)	227 (5.2)	386 (8.9)
Omega-3 fatty acids	263 (6.1)	324 (7.5)	302 (7.0)	342 (7.9)

At 6-month follow-up, 82.3% of patients were prescribed lipid-lowering combination therapy with a statin and another lipid-lowering agent, primarily ezetimibe (*Table 2*). This combination was used in 81.0% of patients, while the combination of statin + ezetimibe + bempedoic acid was used in 6.7% of patients.

In the category of patients at particularly high risk, such as those with diabetes mellitus (1171 patients), we observed a relevant increase in the percentage of patients with LDL-C at goal according to the current guidelines: from 43.4% at baseline to 65.5% at the follow-up visit at 6 months (see Supplementary material online, *Figure S5*).

Variables independently associated with non-attainment of the LDL-C goal included a history of CBVD, hypercholesterolaemia or heart failure, female sex, and the use of fewer lipid-lowering drugs (*Table 3*). Conversely, LDL-C at entry <55 mg/dL and the presence of diabetes mellitus were associated with a higher rate of patients at goal.

In the total population, 222 patients (5.1%) were not prescribed a statin at 6 months. Partial or complete statin intolerance was observed in 194 patients (4.5%) (*Figure 3*). Reasons for not prescribing a statin included total intolerance, contraindication, patient refusal, or physician decision. At the end of the 6-month follow-up visit, 229 (5.3%) patients were prescribed a low-dose statin. The reasons for prescribing a low-dose statin were partial intolerance, medical decision, or patient preference. (see Supplementary material online, *Table S2*). There were no relevant differences in baseline characteristics, comorbidities, or risk factors between patients on statins and patients with complete or partial intolerance (see Supplementary material online, *Table S3*).

In the statin-intolerant group, the proportion of patients with LDL-C < 55 mg/dL increased from 30.4% at baseline to 46.9% at 6 months.

Figure 4 provides a summary of the results on the secondary endpoints of the study. Regarding BP, 51.8% of patients at

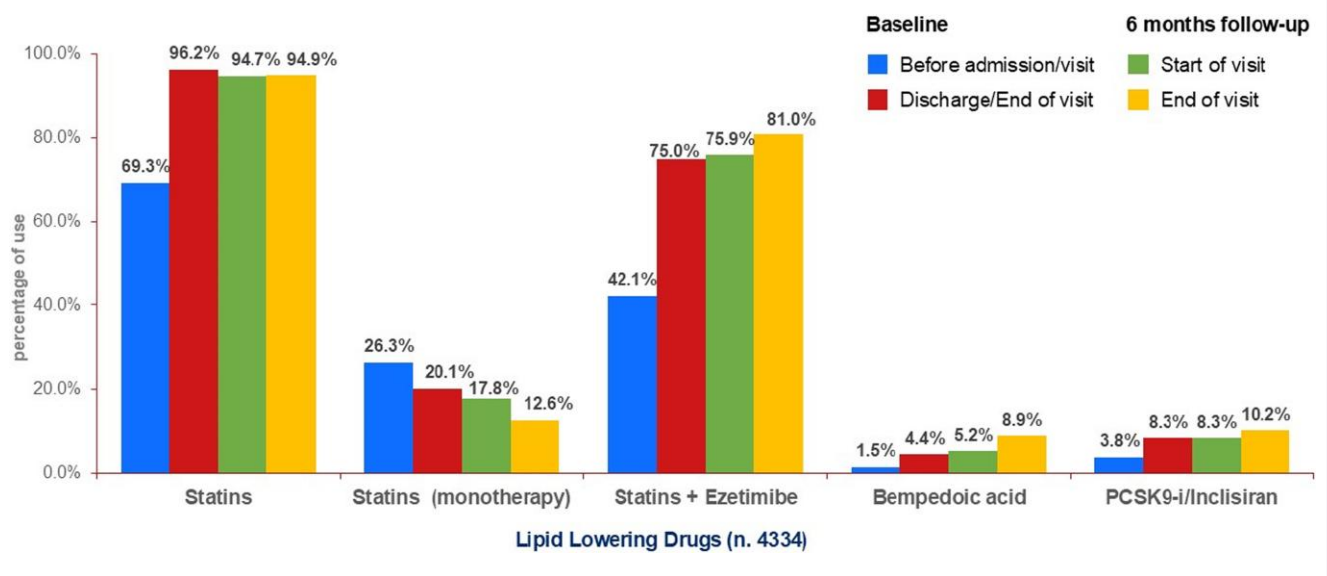


Figure 1 Lipid-lowering drug combination at baseline and at 6-months follow-up.

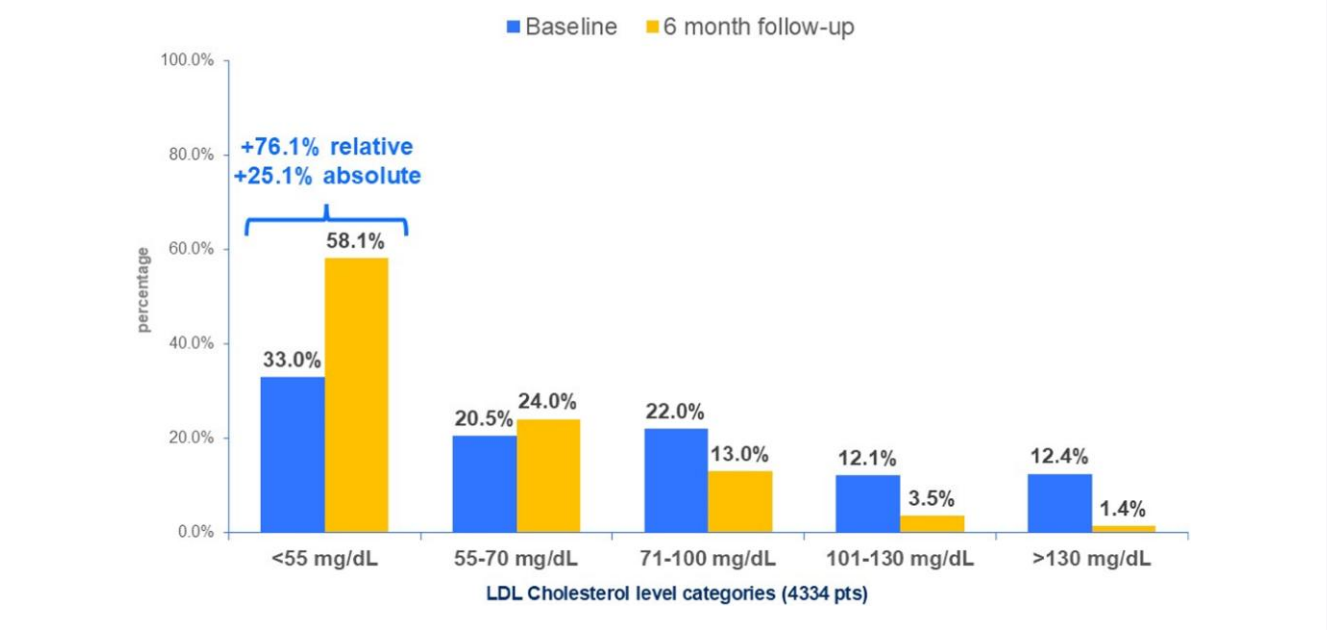


Figure 2 LDL-cholesterol level at baseline and at the 6-months follow-up evaluation.

baseline were within the target range (SBP <130 mmHg). This proportion increased to 57.3% at the 6-month follow-up. HbA1c control at 6 months was performed in just 64.1% of patients with a diabetes mellitus diagnosis. Of those patients for whom an HbA1c measurement was available at 6 months, just 47.0% were within the target range of <7%, a proportion similar to that reported at baseline (43.3%). No significant changes were observed between baseline and the 6-month follow-up in terms of patients with a BMI >27 kg/m² or >30 kg/m². Finally, the proportion of active smokers decreased from 22.1% at baseline to 12.5% at 6 months.

Discussion

The key findings of this study can be summarized as follows (*Graphical abstract*):

Table 3 Logistic regression on LDL-cholesterol goal non-attainment

	OR [95% CI]	*P* value
Previous CAD	—	NS
Previous CBVD	1.43 [1.07–1.93]	0.02
Gender (F vs. M)	1.35 [1.15–1.59]	0.0003
Age (as continuous variable)		NS
Diabetes mellitus	0.66 [0.57–0.77]	<0.0001
History of hypercholesterolemia	1.62 [1.35–1.94]	<0.0001
History of heart failure	1.39 [1.14–1.69]	0.001
Depression	—	NS
Yes vs. no		
Unknown vs. no		
LDL-cholesterol at baseline <55 mg/dL	0.28 [0.24–0.32]	<0.0001
Triglycerides at baseline ≤150 (yes vs. no/unknown)	NS	NS
Number of lipid-lowering drugs prescribed at baseline		<0.0001
0 vs. >2	8.84 [338–23.16]	
1 vs. >2	2.09 [1.61–2.71]	
2 vs. >2	1.36 [1.08–1.72]	

CAD, coronary artery disease; CBVD, cerebrovascular disease; CI, confidence interval; F, female; M, male; OR, odds ratio.

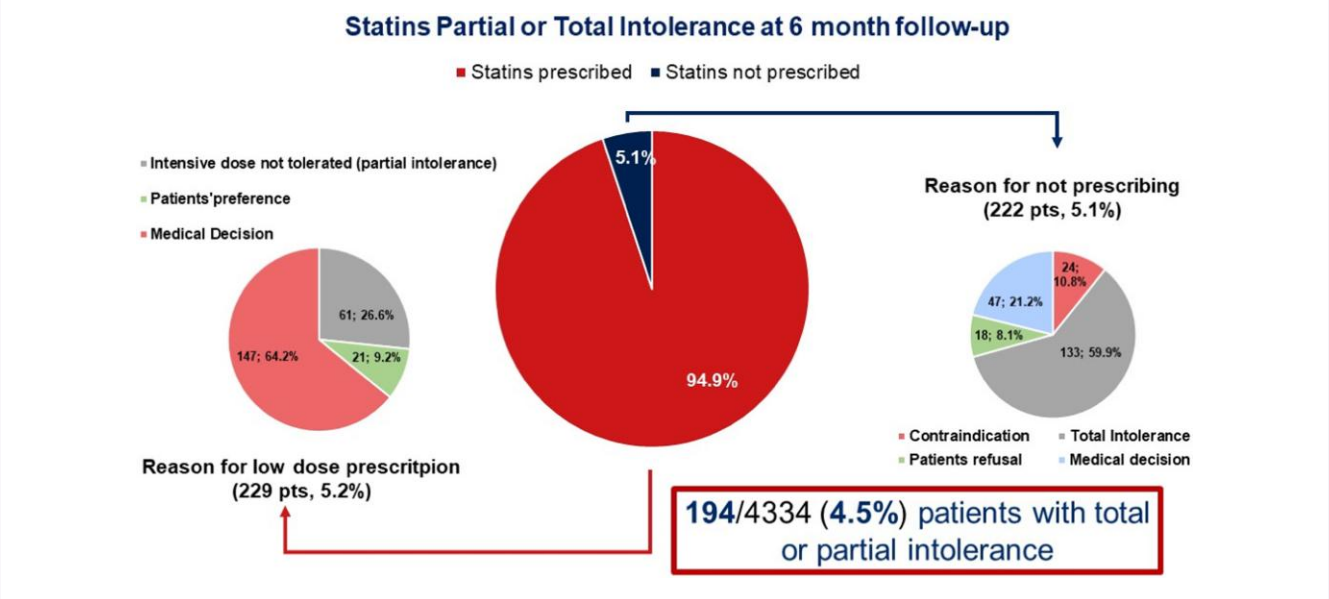


Figure 3 Percentage and reasons of partial and total intolerance to statins at 6-months follow-up.

- the primary objective of the BRING-UP Prevention study was to increase the percentage of patients with LDL-C < 55 mg/dL, as recommended by international guidelines for patients in secondary prevention.[6,7,22] The percentage of patients with LDL-C < 55 mg/dL increased from 33% at discharge/end of visit to 58% at 6 months, representing an absolute increase of 25% and a relative increase of 76%;
- these results were obtained in a context in which most patients were treated with statins at discharge/end of visit, and this treatment was maintained at the 6-month follow-up. Statins were used at high doses in the majority of patients and in combination with ezetimibe in more than three-quarters of patients. The need to use additional drugs was limited to a small number of patients;
- the rate of patients with partial or total intolerance to statins was low and similar to that shown in randomized clinical trials conducted using a double-blind design.
- differently from another recent experience,[23] the lipid-lowering therapeutic strategy adopted in BRING-UP Prevention is easy to manage and certainly affordable, providing a benefit to patients and to the cost of the NHS;

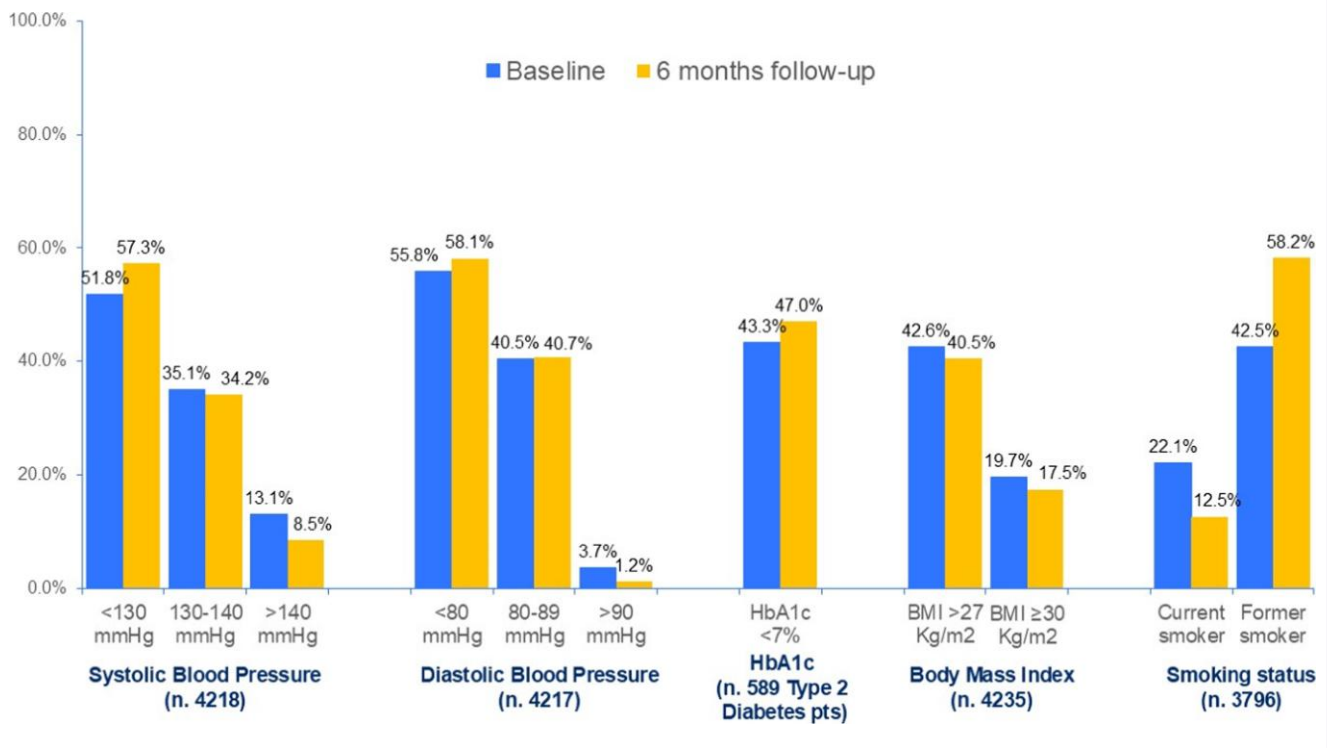


Figure 4 Results on the secondary end-points.

- conducting observational studies aimed at improving physicians' adherence to guidelines can yield important effects on LDL-C control even in the short term. This is especially true when the initiative has the potential to involve a very large and representative number of cardiology units of any technological level across Italy, as in the case of the BRING-UP Prevention study.

Over the past few years, numerous international and Italian registries have documented that the percentage of patients at goal for LDL-C was far from what is recommended by the guidelines.[16,17,24-27]

The EuroAspire V study (2018, 27 countries),[24] conducted in selected cardiology centres focused on prevention, showed progress over previous editions, yet only 29% of patients met LDL-C targets. This is discouraging, given the study goal was 70 mg/dL, higher than the current 55 mg/dL recommendation.

The DA VINCI study (2017–2018)[25] found that most European patients (84%) received statin monotherapy and only 10% combination therapy. Consequently, 55% met 2016 ESC/EAS targets, while just 33% would meet the stricter 2019 goals.

The SANTORINI study (2021–2022)[26] revealed that 80% of high and very high-risk patients still failed to reach 2019 ESC/EAS LDL-C targets across various clinical settings.

In Italy, the POSTER registry (2016–2018)[27] showed that 49% of patients with prior atherothrombotic events achieved the 70 mg/dL goal.

The BRING-UP Prevention study shows a completely different scenario: in patients with a previous atherothrombotic event, who are considered to be at very high risk, the initial education programme and subsequent guided data collection was able to improve the rate of patients on goal from 33% at baseline to 58% at the 6-month follow-up visit, considering the goal of 55 mg/dL. If we look at the previous goal of 70 mg/dL, the rate of patients achieving that goal at 6 months was 82% and this was mainly achieved with a high-intensity statin strategy in combination with ezetimibe. While the use of more recent, costly lipid-lowering drugs was limited, an increasing trend in prescriptions at the six-month follow-up was observed. In order to further improve the proportion of patients reaching their target, the use of these drugs will probably increase in the future. The fact that the goal was even more clearly achieved in patients discharged after an ACS episode compared to outpatients once again demonstrates that the time of discharge is the ideal time to plan and prescribe the appropriate secondary prevention therapies. This approach of limiting the delay between the ACS episode and the prescription of recommended lipid-lowering drugs may ensure a more rapid reduction in LDL-C levels, with the potential consequence of preventing recurrent ACS episodes in the short term and improving adherence to prescribed therapies.

With respect to the secondary endpoints, the proportion of patients with a SBP level at goal (<130 mmHg) increased smoothly at the 6-month follow-up. However, considering the target values recommended by previous guidelines (below 140 mmHg), 82.9% of patients had an SBP below this level.

The most disappointing observation was made in the management of diabetes mellitus. HbA1c was measured in less than two-thirds of patients with diabetes at 6 months, and of these patients, less than 50% were on target. There needs to be more concrete collaboration between diabetologists and cardiologists, particularly for patients at very high risk. New therapeutic options for these patients, such as GLP-1 RA and/or SGLT2 inhibitors, should be used more widely to increase the proportion of patients with appropriate metabolic control and, more importantly, to reduce the risk of future cardiovascular events. The limited follow-up period could explain why no

relevant differences were observed between baseline and the 6-month follow-up regarding body weight control. The introduction of more recent therapeutic options for treating obesity, such as GLP-1 RAs, could provide an additional treatment option for these patients.

Finally, the proportion of active smokers decreased by nearly 10% at the 6-month follow-up. This favourable trend could be due to the fact that approximately half of the patients were recently admitted to hospital, where they were given secondary prevention recommendations for the first time or had them reinforced.

A final consideration should be addressed to this model of implementation science. The success of this model, already demonstrated in previous studies,[18-20] is based on the following aspects: (i) the invitation to participate in the project to a very large and representative setting of cardiology centres, distributed throughout the country and representing all levels of hospital complexity; (ii) the educational programme, based on current guidelines, but also on the potential clinical and logistical barriers to their implementation in clinical practice, with a discussion of how to overcome these barriers; (iii) patient data collection on a web-based system that, if there is a specific indication for a treatment but that treatment is not found to be prescribed, reminds the responsible cardiologist of the guideline recommendation and the reason for any nonprescription should be reported. This is perhaps the most relevant aspect of the model.

Persistence and long-term adherence in secondary prevention are major issues, as it is well documented that a significant proportion of patients do not adhere to treatment over a long period of time. For this reason, the major challenge for the future will be to sustain—and possibly further improve—the results achieved, ensuring a long-term high proportion of patients reaching target levels in one of the most important domains of secondary prevention, namely LDL-C as recommended by current guidelines, while also maintaining close attention to all other secondary prevention targets, including hypertension, diabetes, weight, and smoking. The 12-month follow-up results and the second phase of the project are underway to verify the maintenance or improvement of the 6-month results.

Limitations

Some limitations of our work must be acknowledged and should be addressed as follows: (i) No *ad hoc* validation of consecutive enrolment was performed, and this limitation should be overcome in the future by reviewing administrative data based on hospital records; (ii) The results reflect prescribing behaviour in a cardiology care setting, whereas secondary prevention strategies can be managed in primary care, by internists, or geriatricians; (iii) Many participating sites (30.7%) had a structured secondary prevention clinic or rehabilitation centres, which may have influenced the overall high performance; (iv) Data on underserved populations were not specifically collected; (v) The proportion of women in our project is low and similar to that observed in other trials and observational studies. This is a real issue in the cardiology setting that needs to be addressed in the future; (vi) the improvement in achieving LDL-C goals in patients recently admitted for ACS could be due to the implementation programme as well as the event itself; (vii) no detailed information on patient adherence or motivation was collected.

Conclusions

The BRING-UP Prevention study has achieved its primary goal of a clinically relevant increase in the percentage of patients who achieve their LDL-C targets. Unlike other studies, BRING-UP Prevention demonstrates that this goal can be achieved using well-established, low-cost therapies. For the vast majority of patients, this involves high-intensity statins in combination with ezetimibe. This strategy is particularly effective in achieving LDL-C goals in patients discharged from the hospital after an ACS, confirming the concept of 'strike early, strike easy, strike strong and be sustainable' and limiting the use of more potent and costly lipid-lowering agents to the small proportion of patients who are far from the recommended goal. The favourable results seen at 6 months need to be confirmed over longer periods of time. The 12-month follow-up and the second phase of data collection will confirm whether this implementation science initiative is truly able to improve secondary prevention strategies to reduce LDL-C in patients with a prior atherothrombotic event in a very large cardiology community, well-representing the entire country.

Supplementary material

Supplementary material is available at *European Heart Journal—Quality of Care and Clinical Outcomes* online.

Acknowledgements

We would like to thank the participating patients for their contribution to the study, the study investigators and local site staff who assisted with its conduct, the Regulatory Department at ANMCO Research Centre (Andrea Lorimer and Ilaria Cangioli) and Barbara Bartolomei Mecatti for editorial assistance.

Funding

The sponsor of the study was the Heart Care Foundation, a non-profit, independent organization, which also owns the database. Database management, quality control of the data, and data analyses were under the responsibility of the ANMCO Research Centre of the Heart Care Foundation. The study was funded by Heart Care Foundation with partial unrestricted support from Amgen, Daiichi Sankyo Italia, and Novartis Farma SpA.

No compensation was provided to participating sites, investigators, or members of the Steering Committee. The Steering Committee of the study had full access to all of the data of this study and is taking complete responsibility for the integrity of the data and the accuracy of the data analysis. The author(s) meet criteria for authorship as recommended by the International Committee of Medical Journal Editors (ICMJE).

Author contributions

Author Contributions

Furio Colivicchi (Conceptualization, Funding acquisition, Investigation, Writing—original draft, Writing—review & editing), Pier Luigi Temporelli (Visualization. Writing—review & editing), Francesco Fattirolli (Writing—review & editing), Maurizio Giuseppe Abrignani (Writing—review & editing), Alessandro Alonzo (Investigation. Writing—review & editing), Marcello Arca (Visualization, Writing—review & editing), Maurizio Averna (Writing—review & editing), Daniele Bertoli (Investigation. Writing—review & editing), Paolo Calabrò (Investigation, Writing—review & editing), Leonardo Calò

(Investigation, Writing—review & editing), Stefano Carugo (Investigation, Writing—review & editing), Alberico Luigi Catapano (Visualization, Writing—review & editing), Martina Ceseri (Project administration, Writing—review & editing), Stefania Angela Di Fusco (Investigation, Writing—review & editing), Andrea Di Lenarda (Investigation, Writing—review & editing), Gianna Fabbri (Writing—original draft, Writing—review & editing), Michele Massimo Gulizia (Writing—review & editing), Giuseppe La Rosa (Investigation, Writing—review & editing), Donata Lucci (Data Curation, Formal analysis, Validation, Writing—review & editing), Simone Maffei (Investigation, Writing—review & editing), Alessandro Navazio (Investigation, Writing—review & editing), Fabrizio Oliva (Conceptualization, Funding acquisition, Investigation, Writing—review & editing), Francesco Orso (Conceptualization, Validation, Visualization, Writing—original draft, Writing—review & editing), Carmine Riccio (Investigation, Writing—review & editing), Nicola Scelza (Investigation, Writing—review & editing), Domenico Gabrielli (Conceptualization, Funding acquisition, Investigation, Writing—review & editing), and Aldo Pietro Maggioni (Conceptualization, Funding acquisition, Validation, Writing—original draft, Writing—review & editing)

Conflict of interest: F.C., G.F., M.G.A., S.A.D.F., A.D.L., F.F., M.M.G., C.R., P.L.T., A.A., D.B., P.C., L.C., S.C., G.L.R., S.M., A.N., N.S. have no conflict of interest to disclose. F.O. received personal fees from AstraZeneca, Novartis, Boehringer, Bayer, Menarini, Amgen, Sanofi, Novonordisk, and participation in committees of studies sponsored by Novartis, Boehringer, Bayer, Sanofi, Amgen, AstraZeneca, Novonordisk, not related to the current study. M.C., D.L., and F.O. are employees of Heart Care Foundation, Florence, Italy. M.Arca has nothing to disclose with respect to the present manuscript. Outside the present work had grants from Amryt/Chiesi, Amgen, Daiichi-Sankyo, Lilly, Novartis, Pfizer, Regeneron, Sanofi, Sobi, Ultragenix, Viatris, Ionis; consulting fees from Amryt, Ionis, Daiichi-Sankyo, Novartis, Ultragenix, Amarin; honoraria for lectures, or speaker bureau from Amryt/Chiesi, Amgen, Daiichi-Sankyo, Ionis, Novartis, Regeneron, Sanofi, Ultragenix, Viatris; support for meeting and/or travel from Amryt, Daiichi-Sankyo; Receipt of equipment, materials, drugs, medical writing, gifts or other services from Daiichi-Sankyo, Amgen, Amryt. M.Averna has nothing to disclose with respect to the present manuscript. Outside the present work, had consulting fees from Amarin, Daichii, New Amsterdam, Ultragenyx, and was a member of the Milos Steering Committee. D.G. is the President of Heart Care Foundation; he has nothing to disclose with respect to the present manuscript. Outside the present work had consulting fees from Amgen, Amaryn, and Aurora Biofarma. A.L.C. has nothing to disclose with respect to the present manuscript. Outside the present work, received grants and/or honoraria for lectures, consultancy, or speaker bureau from Amarin, Amgen, Amryt Pharma, Astrazeneca, Daiichi Sankyo, Esperion, Ionis Pharmaceutical, Medscaper, Menarini, Merck, Novartis, NovoNordisk, Peervoice Pfizer, Recordati, Regeneron, Sandoz, Sanofi, The Corpus, Ultragenyx, and Viatris. A.P.M. received personal fees for participation in committees of studies sponsored by AstraZeneca, Bayer, Novartis, and Sanofi, not related to the current study.

Data availability

The data underlying this article will be shared on reasonable request to the BRING-UP Prevention Steering Committee.

BRING-UP Prevention Investigators

Furio Colivicchi, Aldo P. Maggioni, Maurizio Giuseppe Abrignani, Marcello Arca, Maurizio Averna, Alberico Luigi Catapano, Stefania Angela Di Fusco, Andrea Di Lenarda, Francesco Fattirolli, Domenico Gabrielli, Michele Massimo Gulizia, Fabrizio Oliva, Carmine Riccio, Pier Luigi Temporelli, Martina Ceseri, Gianna Fabbri, Giampietro Orsini, Donata Lucci, Lucio Gonzini, Francesca Bianchini, Ester Baldini, Laura Sarti, Furio Colivicchi, Stefania Angela Di Fusco, Alessandro Alonzo, Alessandro Aiello, Stefano Carugo, Lucia Barbieri, Valeria Borrelli, Francesco Manca, Stefano Righini, Angelo Palermo, Paolo Calabrò, Arturo Cesaro, Carmine Riccio, Leonardo Calò, Germana Panattoni, Ilaria Jacomelli, Nicola Vitulano, Maria Scarcia, Vera Perniciaro, Giuliana Germana Mombelli, Francesco Vicari, Antonia Alberti, Ignazio Maria Smecca, Giuseppe Schembri, Manuela Stancampiano, Rita Cristina Myriam Intravaia, Alessandro Maloberti, Chiara Tognola, Marina Delfini, Stefano Iosi, Maria Chiara Gatto, Francesca Moschella Orsini, Giuseppe La Rosa, Antonio Cafà, Gerardo De Mitri, Benedetta Veronesi, Lidia Rossi, Leonardo Grisafi, Michele Emdin, Alberto Aimo, Simone Calcagno, Giulio Luciani, Eduardo Capuano, Chiara Iannarella, Emilio Di Lorenzo, Francesca Lanni, Francesco Greco, Saverio Alberti, Giulia Ricci Lucchi, Matteo Schinzari, Marco Froldi, Marco Proietti, Valentina Pescatore, Erica Brugin, Filippo Maria Sarullo, Antonino Zarcone, Filippo Zilio, Michela Saltori, Matteo Rocco Reccia, Martina Marinelli, Gaetano Povolo, Francesca Saladini, Christian Piergentili, Federica Mondin, Elisabetta Catellani, Antonella Piazza, Carloalberto Biolé, Matteo Bianco, Serafina Valente, Enrica Vitale, Marzia De Biasio, Stefano Poli, Marzia Bertolazzi, Francesco Donati, Nicola Scelza, Adriana Pertegato, Donatella Armata, Antonio Fatta, Marco Triggiani, Simonetta Scalvini, Angelo Carlo Cinelli, Maurizio Bussotti, Lorena Grano De Oro, Laura Francesca Valagussa, Alessandra Giovanna Frattola, Umberto Camaiora, Simone Geroldi, Simone Maffei, Lorena Scappini, Gaia Chiara Selvaggia Magnaghi, Noemi Bruno, Antonio Terranova, Giovanna Liuzzo, Alessia D'Aiello, Michele Ciccarelli, Francesco Loria, Massimo Piepoli, Sara Lucibello, Daniele Bertoli, Riccardo Scattina, Alfredo Posteraro, Annalisa Chiarelli, Luigi Sommariva, Michelangelo Luciani, Pietro Scicchitano, Francesco Massari, Giovanni Cioffi, Elisa Andrenacci, Francesco Monti, Claudio Bilato, Chiara Dalla Valle, Paolo Costa, Luana Sirugo, Pasquale Caldarola, Lucia Sublimi Saponetti, Fiorenza Pia Napolitano, Alessandro De Lorenzis, Gianmarco Iannopollo, Alice Vitagliano, Priscilla Milewski, Roberto Cemin, Marco Corda, Claudia Scudu, Andrea Bianco, Elena Agus, Francesco Perone, Fausto Di Stasio, Anna Picozzi, Salvatore Scarantino, Alessio Gaetano La Manna, Ornella Zaffarana, Michele Capriolo, Umberto Annone, Ilaria Luigia Nalin, Alessandro Pietro Antonio De Santis, Simona D'orazio, Paolo Angori, Francesca Giordana, Lucia Coppini, Felice Achilli, Luisa Chiappa, Gabriele Guardigli, Paolo Cimaglia, Costanza Burgisser, Maria Vittoria Silverii, Natale Daniele Brunetti, Francesco Mautone, Aldo Russo, Maria Federica Zelano, Daniela Sparta', Sonia Mansi, Massimo Pistono, Fabiana Isabella Gambarin, Deborah Cosmi, Euro Antonio Capponi, Salvatore Montalto, Donatella Trigona, Antonio Duca, Ilaria Boretti, Laura Garatti, Giovanni Amedeo Tavecchia, Marta Rescaldani, Sara Goletto, Filippo Trombara, Michele Della Rocca, Andrea Alessandro Moraschi, Verdiana Cirillo, Stefania Sansoni, Cristina Zoccali, Ciro Mauro, Alfredo Madrid, Gennaro Ratti, Antonello D'Andrea, Mario Pacileo, Vincenzo Polizzi, Benedetta La Fata, Giovanni Forni, Bruna Girardi, Francesco Notaristefano, Domenico Di Clemente, Eugenio Genovesi, Duccio Rossini, Luigia Garritano, Daniela Aschieri, Elena

Ferdenzi, Chiara Bernelli, Annamaria Nicolino, Alex Micanti, Gianluigi Tagliamonte, Alfonso Sforza, Anna Frisinghelli, Eleonora Loforese, Andrea Gardi, Michele Fabrizio, Emanuele Barbato, Giovanna Gallo, Elisa Leiballi, Valeria Leonelli, Michele Roberto Di Muro, Roberto Trotta, Maurizio Anselmi, Anna Cima, Giuseppe Di Stolfo, Sandra Mastroianno, Daniela Pavan, Tamara Durat, Maria Carolina Russo, Claudia Calvanese, Gavino Casu, Giovanni Lorenzoni, Walter Sacco, Pietro Alberto Ceresoli, Camilla Facchini, Carlotta Perego, Luca Paolo Alberti, Anna Nancy John, Silvia Polini, Giuseppe Musumeci, Iris Parrini, Maurizio Bertaina, Pierluigi Sbarra, Luisa Mattei, Chiara Cappelletto, Antonio Aloia, Rosamaria Grompone, Sakis Themistoclakis, Ada Cutolo, Maria Grazia Gaspari, Pietro Iodice, Biagio Bosco, Federico Nardi, Claudio Russo, Maria Francesca Marchetti, Elisabetta Scanziani, Vincenzo Crisci, Vincenzo Pernice, Cinzia Galizia, Giuseppina Novo, Ada Sacchi, Carlo Cicerone, Antonino Granatelli, Mariateresa Di Dio, Gerardina Lardieri, Marco Masè, Stefania Franco, Antonio Grossi, Edoardo Conte, Francesco Piemonte, Marco Pepe, Maria Teresa Manes, Matteo Ruzzolini, Daniele Nassiacos, Rocco Lagioia, Stefano Urbinati, Cosimo Angelo Greco, Daniela Grasselli, Maria Molfese, Elisa Guerri, Bernardino Tuccillo, Giulio Molon, Domenico Zucco, Michele Massimo Gulizia, Andrea Rubboli, Pierfranco Simone Dellavesa, Andrea Chiocchini, Silvio Saponara, Emanuele Tizzani, Giovanni Napolitano, Vito Pipitone, Francesca Percoco, Vito Maurizio Parato, Valentina Siviero, Andrea Passantino, Mauro Feola, Stefania Marazia, Micaela Capponi, Amelia Ravera, Giovanni Morani, Lara Gombac, Alvaro Spadoni, Franco Del Piccolo, Gian Piero Perna, Onofrio Rossi, Leonardo Di Ascenzo, Fabio Ferrari, Michele De Benedictis, Jacopo Del Meglio, Roberto Spoladore, Francesco Bellini, Berardo Sarubbi, Andrea Rognoni, Stefania Cherubini, Antonella Muscella, Giosuè Mascioli, Roberto Caruso, Nadia Podimani, Giovanni Licciardello, Gian Paolo Giorda, Carlo Piscicelli, Michele Antonio Clemente, Giuseppe Di Stabile, Natale Di Belardino, Giuseppe Diaferia, Alessandro Lipari, Paolo Compagnucci, Cristina De Colle, Maria Elena Rovere.

References

1. World Heart Federation. *World Heart Report 2023: Confronting the World's Number One Killer*. Geneva: World Heart Federation, 2023.
2. World Health Organization. Cardiovascular diseases (CVDs); Key facts. https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds). Published 2021 (17 Feb 2025)
3. Roth GA, Mensah GA, Johnson CO, Addolorato G, Ammirati E, Baddour LM, *et al.* Global burden of cardiovascular diseases and risk factors, 1990–2019: update from the GBD 2019 study. *J Am Coll Cardiol* 2020;**76**:2982–3021.
4. World Health Organization. Global Atlas on Cardiovascular Disease Prevention and Control. Available from: https://www.who.int/publications/i/item/9789241564373 (20 Feb2025.)
5. Goff DC Jr, Khan SS, Lloyd-Jones D, Arnett DK, Carnethon MR, Labarthe DR, *et al.* Bending the curve in cardiovascular disease mortality: Bethesda + 40 and beyond. *Circulation* 2021;**143**:837–851.
6. Vrints C, Andreotti F, Koskinas KC, Rossello X, Adamo M, Ainslie J, *et al.* 2024 ESC guidelines for the management of chronic coronary syndromes. *Eur Heart J* 2024;**45**:3415–3537.
7. Visseren FLJ, Mach F, Smulders YM, Carballo D, Koskinas KC, Bäck M, *et al.* 2021 ESC guidelines on cardiovascular disease prevention in clinical practice. *Eur Heart J* 2021;**42**:3227–3337.
8. Marx N, Federici M, Schütt K, Müller-Wieland D, Ajjan RA, Antunes MJ, *et al.* 2023 ESC guidelines for the management of cardiovascular disease in patients with diabetes. *Eur Heart J* 2023;**44**:4043–4140.
9. O'Connor EA, Evans CV, Rushkin MC, Redmond N, Lin JS. Behavioral counseling to promote a healthy diet and physical activity for cardiovascular disease prevention in adults with cardiovascular risk factors: updated evidence report and systematic review for the US preventive services task force. *JAMA* 2020;**324**:2076–2094.
10. Miller V, Nambiar L, Saxena M, Leong D, Banerjee A, Werba JP, *et al.* Exploring the barriers to and facilitators of using evidence-based drugs in the secondary prevention of cardiovascular diseases: findings from a multistakeholder, qualitative analysis. *Glob Heart* 2018;**13**:27–34.e17.
11. Banerjee A, Khandelwal S, Nambiar L, Saxena M, Peck V, Moniruzzaman M, *et al.* Health system barriers and facilitators to medication adherence for the secondary prevention of cardiovascular disease: a systematic review. *Open Heart* 2016;**3**:e000438.
12. Holtrop J, Bhatt DL, Ray KK, Mach F, Smulders YM, Carballo D, *et al.* Impact of the 2021 European society for cardiology prevention guideline's stepwise approach for cardiovascular risk factor treatment in patients with established atherosclerotic cardiovascular disease. *Eur J Prev Cardiol* 2024;**31**:754–762.
13. Kreutz R, Brunström M, Burnier M, Grassi G, Januszewicz A, Muiesan ML, *et al.* 2024 European society of hypertension clinical practice guidelines for the management of arterial hypertension. *Eur J Intern Med* 2024;**126**:1–15.
14. Mach F, Koskinas KC, van Lennep JE R, Tokgözoğlu L, Badimon L, Baigent C, *et al.* 2025 focused update of the 2019 ESC/EAS guidelines for the management of dyslipidaemias. *Eur Heart J* 2025;**46**:4359–4378.
15. Maggioni AP, Calabria S, Rossi E, Martini N; on the behalf of the ARNO Observatory. Use of lipid lowering drugs in patients at very high risk of cardiovascular events: an analysis on nearly 3,000,000 Italian subjects of the ARNO observatory. *Int J Cardiol* 2017;**246**:62–67.
16. Calabria S, Ronconi G, Dondi L, Piccinni C, Cinconze E, Pedrini A, *et al.* Coronary artery disease in patients older than 35 and eligible for cardiovascular secondary prevention: an Italian retrospective observational analysis of healthcare administrative databases. *J Clin Med* 2021;**10**:4708.
17. Arca M, Calabrò P, Solini A, Pirillo A, Gambacurta R, Ray KK, *et al.* Lipid-lowering treatment and LDL-C goal attainment in high and very high cardiovascular risk patients: evidence from the SANTORINI study-the Italian experience. The SANTORINI Italian subgroup study. *EAJ* 2023;**1**:1–13.
18. Maggioni AP, Sinagra G, Opasich C, Geraci E, Gorini M, Gronda E, *et al.* Beta blockers in patients with congestive heart failure: guided use in clinical practice investigators. Treatment of chronic heart failure with beta adrenergic blockade beyond controlled clinical trials: the BRING-UP experience. *Heart* 2003;**89**:299–305.
19. Opasich C, Boccanelli A, Cafiero M, Cirrincione V, Sindaco DD, Lenarda AD, *et al.* Programme to improve the use of beta-blockers for heart failure in the elderly and in those with severe symptoms: results of the BRING-UP 2 study. *Eur J Heart Fail* 2006;**8**:649–657.
20. Gulizia MM, Orso F, Mortara A, Lucci D, Aspromonte N, De Luca L, *et al.* BLITZ-HF: a nationwide initiative to evaluate and improve adherence to acute and chronic heart failure guidelines. *Eur J Heart Fail* 2022;**24**:2078–2089.
21. Colivicchi F, Fabbri G, Oliva F, Abrignani MG, Arca M, Averna M, *et al.* LDL-cholesterol levels and lipid lowering therapy in secondary prevention. Baseline data from the BRING-UP prospective registry. *Int J Cardiol* 2025;**433**:133290.
22. Knuuti J, Wijns W, Saraste A, Capodanno D, Barbato E, Funck-Brentano C, *et al.* 2019 ESC guidelines for the diagnosis and management of chronic coronary syndromes. *Eur Heart J* 2020;**41**:407–477.
23. Gargiulo P, Basile C, Galasso G, Bellino M, D'Elia D, Patti G, *et al.* Strike early-strike strong lipid-lowering strategy with proprotein convertase subtilisin/kexin type 9 inhibitors in acute coronary syndrome patients: real-world evidence from the AT-TARGET-IT registry. *Eur J Prev Cardiol* 2024;**31**:1806–1816.
24. De Backer G, Jankowski P, Kotseva K, Mirrakhimov E, Reiner Ž, Rydén L, *et al.* Management of dyslipidaemia in patients with coronary heart disease: results from the ESC-EORP EUROASPIRE V survey in 27 countries. *Atherosclerosis* 2019;**285**:135–146.
25. Ray KK, Molemans B, Schoonen WM, Giovas P, Bray S, Kiru G, *et al.* EU-wide cross-sectional observational study of lipid-modifying therapy use in secondary and primary care: the DA VINCI study. *Eur J Prev Cardiol* 2021;**28**:1279–1289.
26. Ray KK, Haq I, Bilitou A, Manu MC, Burden A, Aguiar C, *et al.* Treatment gaps in the implementation of LDL cholesterol control among high- and very high-risk patients in Europe between 2020 and 2021: the multinational observational SANTORINI study. *Lancet Reg Health Eur* 2023;**29**:100624.
27. Gulizia MM, Maggioni AP, Abrignani MG, Bilato C, Mangiacapra F, Sanchez FA, *et al.* Prevalence of familial hypercholeSTerolaemia (FH) in Italian patients with coronary artERy disease: the POSTER study. *Atherosclerosis* 2020;**308**:32–38.