Received: 3 February 2018 | Revised: 10 March 2018 | Accepted: 27 March 2018

DOI: 10.1002/clc.22955

PREVENTION WILEY CLINICAL CARDIOLOGY

CLINICAL INVESTIGATIONS

Achievement of multiple therapeutic targets for cardiovascular disease prevention: Retrospective analysis of real practice in Italy

Ilaria Figliuzzi[1] | Vivianne Presta[1] | Barbara Citoni[1] | Francesca Miceli[1] | Francesca Simonelli[1] | Allegra Battistoni[1] | Roberta Coluccia[2] | Andrea Ferrucci[1] | Massimo Volpe[1,2] | Giuliano Tocci[1,2]

[1]Division of Cardiology, Department of Clinical and Molecular Medicine, Faculty of Medicine and Psychology, University of Rome Sapienza, Sant'Andrea Hospital, Rome, Italy

[2]IRCCS Neuromed, Pozzilli, Italy

Correspondence
Giuliano Tocci, MD, PhD, Division of Cardiology, Department of Clinical and Molecular Medicine, Faculty of Medicine and Psychology, University of Rome Sapienza, Sant'Andrea Hospital, Rome, Italy
Email: giuliano.tocci@uniroma1.it

Background: Pharmacological therapy in patients at high cardiovascular (CV) risk should be tailored to achieve recommended therapeutic targets.

Hypothesis: To evaluate individual global CV risk profile and to estimate the control rates of multiple therapeutic targets for in adult outpatients followed in real practice in Italy.

Methods: Data extracted from a cross-sectional, national medical database of adult outpatients in real practice in Italy were analyzed for global CV risk assessment and rates of control of major CV risk factors, including hypertension, dyslipidemia, diabetes, and obesity. CV risk characterization was based on the European SCORE equation and the study population stratified into 3 groups: low risk (<2%), intermediate risk (≥2%–<5%), and high to very high risk (≥5%).

Results: We analyzed data from 7158 adult outpatients (mean age, 57.7 ±5.3 years; BMI, 28.3 ±5.0 kg/m^2, BP, 136.0 ±14.3/82.2 ±8.3 mm Hg; total cholesterol, 212.7 ±40.7 mg/dL), among whom 2029 (45.2%) had low, 1730 (24.2%) intermediate, and 731 (16.3%) high to very high risk. Increased SCORE risk was an independent predictor of poor achievement of diastolic BP <90 mm Hg (OR: 0.852, 95% CI: 0.822–0.882), LDL-C < 130 mg/dL (OR: 0.892, 95% CI: 0.861–0.924), HDL-C > 40 (males)/>50 (females) mg/dL (OR: 0.926, 95% CI: 0.895–0.958), triglycerides <160 mg/dL (OR: 0.925, 95% CI: 0.895–0.957), and BMI <25 kg/m^2 (OR: 0.888, 95% CI: 0.851–0.926), even after correction for diabetes, renal function, pharmacological therapy, and referring physicians (P < 0.001).

Conclusions: Despite low prevalence and optimal medical therapy, individuals with high to very high SCORE risk did not achieve recommended therapeutic targets in a real-world practice.

KEYWORDS

Diabetes, Dyslipidemia, European Risk SCORE, Global Cardiovascular Risk, Hypertension, Obesity, Smoking, Therapeutic Targets

1 | INTRODUCTION

Cardiovascular (CV) diseases continue to represent by far the leading cause of morbidity and mortality in various countries, including Italy.[1,2] Several surveys reported persistently low rates of control of major CV risk factors, including hypertension (HTN), hypercholesterolemia, atherogenic dyslipidemia, and diabetes mellitus (DM), in both North American [3] and European[4–7] countries.

A major driver for the insufficient control rates of major CV risk factors often has been related to the relatively low standard of care provided by treating physicians. This seems to be linked, among others, to various factors, including time restrictions during clinical consultations, inadequate knowledge and application of guidelines' recommendations, and lack of application of timely and integrated pharmacological and nonpharmacological interventions.[8,9] For these reasons, implementation of preventive measures has been proposed

as a cornerstone of healthcare policies.[10] In this view, the central role of individual global CV risk stratification has been recently reaffirmed to early identify and promptly treat asymptomatic high-risk individuals and reduce the incidence of CV outcomes, mostly in the setting of primary care.[11]

The Evaluation of Final Feasible Effect of Control Training and Ultra-sensitisation (EFFECTUS) survey showed a very high prevalence of CV risk factors among adult outpatients followed by different groups of Italian physicians, mostly general practitioners (GPs).[12] Further analyses from the same database were performed to detect potentially different approaches according to local disparities,[13] availability of electronic support,[14] and predefined subsets of outpatients, such as those with DM or HTN.[15,16] However, specific analysis testing the achievement of different multiple therapeutic targets according to risk score estimation was not available.

On the basis of these considerations, and in view of the large and representative population sample of this database, we aimed here to evaluate individual global CV risk profile by using the European Systematic Coronary Risk Evaluation (SCORE) risk model and to estimate the control rates of multiple therapeutic targets for HTN, dyslipidemia, obesity, and DM in this large cohort of adult outpatients followed in real practice in Italy.

2 | METHODS

2.1 | Study methodology

The methodology of the study has been previously described.[12] Briefly, the EFFECTUS survey was designed to evaluate prevalence and control rates of major CV risk factors, as well diagnostic opportunities and treatment habits of physicians in a setting of real practice in Italy. The program was addressed to physicians operating in both general practice and outpatient clinics across the entire national territory and was aimed at improving quality standards for cardiovascular disease (CVD) management and control in Italy.

Written invitations were forwarded in a sizable number to ensure a sufficiently representative sample of the study population and to achieve this target within a period of approximately 3 to 4 weeks. For this purpose, each of the 20 to 24 regional referral centers invited 60 physicians per region (35 GPs, 15 cardiologists, and 10 diabetologists) to participate to this survey, for a total of 1400 individual physicians, selected on the basis of the above-mentioned clinical habits and personal characteristics. Then, approximately 1250 invitations were issued and physicians were asked to fill out questionnaires featuring their characteristics and practice (age, sex, geographic location, professional expertise, use of electronic database) and to reply anonymously to the administrative sites of their regional referral centers.

Following their acceptance, involved physicians were asked to report clinical data extracted from their clinical records from 10 consecutive adult Caucasian outpatients age > 40 years, whatever the reason they referred to their own attending physicians. The entire data collection was completed by participants on-site and then delivered to the data-collection center by online access to a remote database. At each study site, collection of data was conducted during 1 week in May 2006. Physicians who completed the program did not receive any compensation for their participation.

2.2 | Data collection

Data collection included full medical history and physical examination. Information was obtained on current therapy for HTN, dyslipidemia, DM, and concomitant CV diseases and comorbidities, including coronary artery disease, stroke, and heart failure, as well as any concomitant medication. Calculation was made of body mass index (BMI), expressed as body weight in kilograms divided by the square of height in meters (kg/m^2). Clinic systolic and diastolic blood pressure (BP) levels, serum levels of total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglycerides (TG), glucose, glycated hemoglobin (HbA1c), and creatinine were extracted from available clinical records. Available data were centrally analyzed for global CV risk evaluation and CV risk profile characterization.

The study conformed to the Declaration of Helsinki and its subsequent modifications and was authorized by the reference ethics committee. The confidentiality of the data was carefully and strictly protected.

2.3 | Definition of risk factors, markers of organ damage, and comorbidities

HTN was defined as systolic BP ≥140 mm Hg and/or diastolic BP ≥90 mm Hg in untreated subjects or in the presence of stable (≥6 months) antihypertensive drug treatment.[17] Diagnosis of hypercholesterolemia was made based on TC levels ≥190 mg/dL, LDL-C levels ≥130 mg/dL, or stable lipid-lowering drug treatment in both conditions.[18–20] Obesity was defined as BMI ≥25 kg/m^2.[21] Finally, DM was defined as fasting plasma glucose levels ≥126 mg/dL.[22–24]

Coronary artery disease was defined according to the presence of acute coronary syndrome.[25–27] Finally, nonfatal stroke was defined as a neurological deficit with sudden onset and persistence of symptoms for >24 hours or leading to death with no apparent causes other than vascular ones.[28] Transient ischemic attack was defined as a neurological event with the signs and symptoms of stroke that resolves within a short period of time (typically lasting 2 to 30 minutes).[29]

Chronic kidney disease (CKD) was defined as eGFR <60 mL/min/1.73 m^2, whereas severe CKD was defined as eGFR <30 mL/min/1.73 m^2 or dialysis.

2.4 | Risk score models

CV risk was estimated by using European SCORE risk equation, which provides the 10-year risk of fatal events for patients age 40 to 65 years.[30] Risk estimation for developing fatal coronary events is based on the following items for the equation: TC, systolic BP, age, and smoking status.[30] The study population was composed of adult Caucasian individuals born and living in Italy; therefore, the low-risk score charts have been applied.[30] Included patients were stratified into 3 groups: low SCORE risk (<2%), intermediate SCORE risk (≥2%–<5%), and high to very high SCORE risk (≥5%).[30]

2.5 | Therapeutic targets

The following therapeutic targets were set for predefined CV risk factors: systolic/diastolic BP <140/90 mm Hg in patients with essential HTN and < 140/85 mm Hg in DM patients with HTN,[17] BMI ≤25 kg/m^2,[21] HDL-C ≥ 40 mg/dL in males and ≥ 50 mg/dL in females,[19,20] TG ≤150 mg/dL,[19,20] and fasting glucose ≤126 mg/dL.[22]

2.6 | Statistical analysis

Data were entered into Microsoft Access for Windows (Microsoft Corp., Redmond, WA). Baseline characteristics of patients are presented as number and percentage for dichotomous variables and mean ±SD for continuous variables. Normal distribution of data was assessed using histograms and the Kolmogorov–Smirnov test. Differences between continuous variables were assessed using ANOVA test. Categorical variables were compared among groups by the χ^2 test. To evaluate the relationship between European SCORE risk and control rates of different therapeutic targets (ie, those not already included in the SCORE risk equation), odds ratios (OR) and 95% confidence intervals (CI) were derived from logistic regression analysis. A multivariable model was fitted with baseline covariates that showed differences at the <0.05 significance level. All tests were 2-sided, and a P value <0.05 was considered statistically significant. All calculations were generated using SPSS software, version 20.0 (IBM Corp., Armonk, NY).

3 | RESULTS

3.1 | Study population

From an overall sample of 16 645 adult outpatients included in the original database, we selected 7158 (43.0%) records with valid clinical data and patient age between 40 and 65 years, among whom the vast majority (77.6%) were followed by GPs. In this sample, 2029 (45.2%) patients had low SCORE risk, 1730 (24.2%) had intermediate SCORE risk, and 731 (16.3%) had high to very high SCORE risk.

3.2 | Distribution of CV risk factors and comorbidities

General characteristics of the study population stratified in different SCORE risk groups are reported in Table 1. There were significantly more male individuals in the intermediate-risk and high-risk categories compared with the low-risk group (P < 0.001). As expected, all CV risk factors, such as sedentary lifestyle, smoking, dyslipidemia, and HTN, as well as associated clinical conditions such as coronary and cerebrovascular diseases, showed a significant trend toward increase from low to high risk categories (P < 0.001 for all comparisons, with the only exception of family history of CVD, P = 0.03). CKD was significantly more prevalent in low-risk individuals compared with other groups (P < 0.001).

Similarly, systolic and diastolic BP levels, TC and LDL-C, TG, glucose, and serum creatinine levels showed a significant trend toward increase from the low-risk category to the high- to very high-risk category, whereas HDL-C levels and eGFR showed a significant reduction from the former to the latter groups of individuals. Indeed, significant correlations with European SCORE risk were observed for all tested variables, including diastolic BP (r = 0.286; P < 0.001), LDL-C (r = 0.221; P < 0.001), HDL-C (r = −0.121; P < 0.001), TG (r = 0.145; P < 0.001), and BMI (r = 0.072; P < 0.001).

3.3 | Pharmacological and nonpharmacological interventions

As illustrated in Table 1, recommendations for smoking cessation, diet, and physical activity were more frequently prescribed in patients in the high-risk categories compared with those at intermediate and low risk (P < 0.001 for all comparisons).

Patients at high to very high risk also received more drug therapies for HTN (P < 0.001) and dyslipidemia (P < 0.001), as well as more antiplatelet agents (P < 0.001), compared with other groups, whereas no significant differences were found among groups with regard to antidiabetic therapy.

3.4 | Achievement of predefined therapeutic targets

Proportions of patients achieving the recommended therapeutic targets for major CV risk factors are reported in Table 2. Control rates of both systolic BP and TC levels were significantly lower in patients at high to very high SCORE risk compared with those at low or intermediate risk (P < 0.001 for both comparisons). Also, proportions of patients achieving the recommended therapeutic targets for additional CV risk, including diastolic BP, LDL-C and HDL-C, TG, BMI, and glucose levels, were significantly lower in the high-risk group than in other groups of outpatients (P < 0.001 for all comparisons). The same trends were also observed in patients under pharmacological therapies (Figure 1). In treated hypertensive patients (n = 4485), among whom 20.4% were in the high-risk group, 1703 (42.0%) achieved the systolic BP goal of <140 mm Hg, 2655 (65.5%) achieved the diastolic BP goal of <90 mm Hg, and 1512 (37.3%) achieved the recommended therapeutic target for BP <140/90 mm Hg. In treated dyslipidemic patients (n = 2442), among whom 21.3% were in the high-risk group, 699 (42.4%) achieved the LDL-C goal of <130 mg/dL. Finally, in treated patients with DM (n = 1887), among whom 17.7% were in the high-risk group, 355 (23.9%) achieved the glucose goal of <126 mg/dL and 86 (6.8%) achieved the HbA1c goal of <6% (available in n = 1960 DM patients).

3.5 | Univariate and multivariate analysis

These analyses are reported in Table 3 for the overall population sample, for patients with DM, and for patients at very high CV risk with previous myocardial infarction or stroke. In the total population, increased SCORE risk resulted an independent predictor of poor achievement of diastolic BP <90 mm Hg (OR: 0.852, 95% CI: 0.822–0.882), LDL-C < 130 mg/dL (OR: 0.892, 95% CI: 0.861–0.924), HDL-C > 40 mg/dL (in males) and > 50 mg/dL (in females; OR: 0.926, 95% CI: 0.895–0.958), TG <160 mg/dL (OR:

TABLE 1 General characteristics of adult outpatients, stratified according to European SCORE

Parameters	Low Risk, n = 2029 (45.2)	Intermediate Risk, n = 1730 (24.2)	High to Very High Risk, n = 731 (16.3)	*P* Value
Female sex	1436 (71.0)	488 (28.2)[a]	61 (8.3)[a,b]	<0.001
Age, y	55.1 ± 5.3	59.8 ±4.0	61.6 ±3.1	<0.001
BMI, kg/m^2	28.1 ±5.3	28.5 ±4.8	28.9 ±4.4	0.003
WC, cm	97.5 ±17.0	100.4 ±14.3	103.8 ±14.4	<0.001
Clinical parameters				
SBP, mm Hg	130.7 ±12.5	137.5 ±12.7	146.7 ±14.4	<0.001
DBP, mm Hg	80.3 ±7.9	82.6 ±7.5	86.1 ±8.5	<0.001
TC, mg/dL	205.0 ±38.0	212.9 ±39.2	230.6 ±42.8	<0.001
HDL-C, mg/dL	52.2 ±13.4	50.4 ±12.7	48.0 ±11.5	<0.001
LDL-C, mg/dL	127.0 ±38.1	133.2 ±37.6	148.3 ±41.3	<0.001
TG, mg/dL	150.9 ±75.0	165.2 ±88.3	178.7 ±78.5	<0.001
Glucose, mg/dL	118.5 ±42.7	122.2 ±42.8	126.3 ±44.2	<0.001
sCr, mg/dL	0.9 ±0.2	1.0 ±0.3	1.1 ±0.3	<0.001
eGFR, mg/mL/1.72 m^2	89.1 ±32.6	94.9 ±64.4	90.4 ±32.7	0.015
CV risk factors				
Fx CVD	622 (30.7)	546 (31.6)	273 (37.3)[a,b]	0.03
Sedentary lifestyle	1399 (69.0)	1144 (66.1)	489 (66.9)	0.169
Smoking	455 (22.4)	712 (41.2)[a]	617 (84.4)[a,b]	<0.001
Dyslipidemia	935 (46.1)	946 (54.7)[a]	471 (64.4)[a,b]	<0.001
HTN	1172 (57.8)	1201 (69.4)[a]	608 (83.2)[a,b]	<0.001
Obesity	1103 (70.2)	1034 (77.2)[a]	478 (83.1)[a,b]	<0.001
DM	664 (32.7)	635 (36.7)[a]	289 (39.5)[a]	0.001
Comorbidities				
CAD	241 (11.9)	358 (20.7)[a]	166 (22.7)[a]	<0.001
MI	160 (7.9)	234 (13.5)[a]	99 (13.5)[a]	<0.001
Angina	79 (3.9)	111 (6.4)[a]	70 (9.6)[a,b]	<0.001
CABG	121 (6.0)	202 (11.7)[a]	70 (9.6)[a]	<0.001
Cerebrovascular disease	48 (2.4)	50 (2.9)	38 (5.2)[a,b]	0.001
Stroke	25 (1.2)	20 (1.2)	14 (1.9)	0.290
TIA	32 (1.6)	28 (1.6)	34 (4.7)[a,b]	<0.001
PAD	112 (5.5)	165 (9.5)[a]	100 (13.7)[a,b]	<0.001
CKD	139 (11.9)	82 (8.1)[a]	29 (6.7)[a]	0.001
Severe CKD	7 (0.3)	2 (0.1)	2 (0.3)	0.194
Nonpharmacological advice				
Smoking cessation	766 (37.8)	859 (49.7)[a]	510 (69.8)[a,b]	<0.001
Weight reduction	1474 (72.6)	1348 (77.9)[a]	578 (79.1)[a]	<0.001
Physical activity	1403 (69.1)	1300 (75.1)[a]	555 (75.9)[a]	<0.001
Drug therapy				
BP-lowering Tx	1314 (64.8)	1351 (78.1)[a]	638 (87.3)[a,b]	<0.001
Lipid-lowering Tx	856 (42.2)	880 (50.9)[a]	440 (60.2)[a,b]	<0.001
Glucose-lowering Tx	638 (31.4)	597 (34.5)[a]	255 (34.9)[a,b]	0.078
Antiplatelet Tx	599 (29.5)	722 (41.7)[a]	403 (55.1)[a,b]	<0.001

Abbreviations: BMI, body mass index; BP, blood pressure; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CKD, chronic kidney disease; CV, cardiovascular; DBP, diastolic blood pressure; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; Fx CVD, family history of cardiovascular disease; HDL-C, high-density lipoprotein cholesterol; HTN, hypertension; LDL-C, low-density lipoprotein cholesterol; MI, myocardial infarction; PAD, peripheral arterial disease; SBP, systolic blood pressure; SCORE, Systematic Coronary Risk Evaluation; sCr, serum creatinine; SD, standard deviation; TC, total cholesterol; TG, triglycerides; TIA, transient ischemic attack; Tx, treatment; WC, waist circumference. Data are presented as n (%) or mean ±SD.

[a] $P < 0.05$ vs low risk.

[b] $P < 0.05$ vs intermediate risk.

0.925, 95% CI: 0.895–0.957), and BMI <25 kg/m^2 (OR: 0.888, 95% CI: 0.851–0.926), even after correction for DM, renal function, pharmacological therapy, and referring physicians ($P < 0.001$). The same results were observed in patients with DM, although European SCORE risk did not predict the achievement of glucose control in this high-risk category. Similarly, SCORE showed no significant predictive

TABLE 2 Control of major CV risk factors in adult outpatients, stratified according to European SCORE

Parameters	Low Risk	Intermediate Risk	High to Very High Risk	*P* Value
Major CV risk factors				
SBP <140 mm Hg	1394 (68.7)	831 (48.0)	172 (23.5)	<0.001
TC <190 mg/dL	657 (32.4)	425 (24.6)	106 (14.5)	<0.001
Additional CV risk factors				
DBP <90 mm Hg	1640 (80.8)	1280 (74)	411 (56.2)	<0.001
LDL-C < 130 mg/dL	960 (56.2)	718 (48.9)	217 (34.7)	<0.001
HDL-C ≥ 40 (M)/ ≥50 (F) mg/dL	937 (53.2)	740 (49.2)	243 (38.2)	<0.001
TG <160 mg/dL	1010 (53.8)	748 (46.9)	238 (35.5)	<0.001
Glucose <126 mg/dL	1336 (71.3)	1072 (67.8)	435 (64.4)	0.002
BMI <25 kg/m^2	468 (29.8)	305 (22.8)	97 (16.9)	<0.001

Abbreviations: BMI, body mass index; CV, cardiovascular; DBP, diastolic blood pressure; F, females; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; M, males; SBP, systolic blood pressure; SCORE, Systematic Coronary Risk Evaluation; SD, standard deviation; TC, total cholesterol; TG, triglycerides. Data are presented as n (%) or mean ±SD. Major risk factors (eg, SBP and TC levels) are included in the European SCORE risk equation, whereas other additional risk factors, such as DBP, LDL-C, HDL-C, TG, and BMI, were not included.

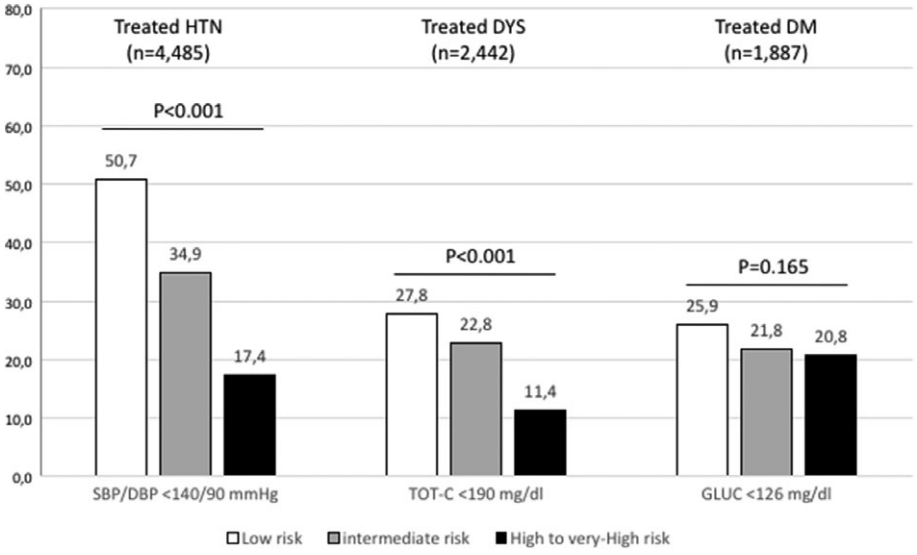

FIGURE 1 Proportions of patients achieving the recommended therapeutic targets for SBP/DBP, total cholesterol, and fasting glucose levels according to European SCORE. Proportions of patients on targets have been calculated among treated patients with HTN, treated patients with DYS, and treated outpatients with DM, respectively. Abbreviations: DBP, diastolic blood pressure; DM, diabetes mellitus; DYS, dyslipidemia; GLUC, glucose; HTN, hypertension; LDL, low-density lipoprotein cholesterol; SBP, systolic blood pressure; SCORE, Systematic Coronary Risk Evaluation; TOT-C, total cholesterol

value of glucose and BMI control in those patients with previous myocardial infarction or stroke.

4 | DISCUSSION

In the present analysis, we applied the European SCORE risk equation to evaluate individual global CV risk profile and estimated rates of control of both conventional and additional CV risk factors in adult outpatients predominantly followed by GPs in a setting of real practice in Italy.

In view of the characteristics of the applied risk score calculator, which cannot be used in people age < 40 years or > 65 years, for the purpose of the present analysis we considered only data from those individuals aged 40 to 65 years. In this sample, we observed high prevalence of all major CV factors, particularly in high-risk and very high-risk categories of adult outpatients, thus confirming the high burden of CVD in the adult population in our country. This high prevalence of risk factors, mostly HTN and hypercholesterolemia, was paralleled by high risk score estimations and relatively low control rates, independently by the presence or absence of pharmacological therapies and other comorbidities. These observations were consistent with previous clinical studies performed on the same database,[12] as well as with other clinical studies performed in the setting of clinical practice in Italy, which reported that the proportions of high-risk patients who achieved the recommended BP targets were relatively low (about 30%).[31,32] As an example, in the European Study on Cardiovascular Risk Prevention and Management in Usual Daily Practice (EURIKA), about 40% of the study population had high SCORE risk; and control rates of major CV risk factors, including HTN, dyslipidemia, DM, and BMI, were similar to those reported in our analysis.[33] The same results were also reported in the European Action on Secondary and Primary Prevention by Intervention to Reduce Events III (EUROASPIRE III),[5] as well as in the National Health and Nutrition Examination Surveys (NHANES).[34]

The failure in achieving the recommended therapeutic targets cannot be explained by poor quality of the clinical data or low awareness of global CV risk estimation, as we observed significant correlations among all tested clinical parameters and SCORE risk estimations. In other words, included physicians had all the requested clinical information for CV risk estimation, and, thus, cannot be unaware of the level of risk of their patients; yet they were not able to achieve the

TABLE 3 Univariate and multivariate analyses for European SCORE risk and the achievement of different therapeutic targets in the overall population sample, in patients with DM, and in patients with previous MI or stroke

Parameters	OR (95% CI)	*P* Value
Overall population, N = 7158		
European SCORE*DBP <90 mm Hg		
Unadjusted	0.833 (0.812–0.854)	<0.001
Adjusted (physicians, DM, BMI, eGFR, antihypertensive Tx)	0.852 (0.822–0.882)	<0.001
European SCORE*LDL-C < 130 mg/dL		
Unadjusted	0.863 (0.840–0.887)	<0.001
Adjusted (physicians, DM, BMI, eGFR, lipid-lowering Tx)	0.892 (0.861–0.924)	<0.001
European SCORE*HDL-C > 40 mg/dL (M) and > 50 mg/dL (F)		
Unadjusted	0.913 (0.890–0.937)	<0.001
Adjusted (physicians, DM, BMI, eGFR, lipid-lowering Tx)	0.926 (0.895–0.958)	<0.001
European SCORE*TG <160 mg/dL		
Unadjusted	0.897 (0.874–0.920)	<0.001
Adjusted (physicians, DM, BMI, eGFR, lipid-lowering Tx)	0.925 (0.895–0.957)	<0.001
European SCORE*Glucose <126 mg/dL		
Unadjusted	0.955 (0.933–0.978)	<0.001
Adjusted (physicians, BMI, eGFR, glucose-lowering Tx)	0.962 (0.918–1.008)	0.100
European SCORE*BMI <25 kg/m^2		
Unadjusted	0.885 (0.854–0.917)	<0.001
Adjusted (physicians, DM, eGFR)	0.888 (0.851–0.926)	<0.001
Patients with DM		
European SCORE*DBP <90 mm Hg		
Unadjusted	0.854 (0.820–0.890)	<0.001
Adjusted (physicians, BMI, eGFR, antihypertensive Tx)	0.860 (0.814–0.908)	<0.001
European SCORE*LDL-C < 130 mg/dL		
Unadjusted	0.868 (0.831–0.907)	<0.001
Adjusted (physicians, BMI, eGFR, lipid-lowering Tx)	0.892 (0.845–0.941)	<0.001
European SCORE*HDL-C > 40 mg/dL (M) and > 50 mg/dL (F)		
Unadjusted	0.936 (0.989–0.975)	0.001
Adjusted (physicians, BMI, eGFR, lipid-lowering Tx)	0.912 (0.862–0.965)	0.001
European SCORE*TG <160 mg/dL		
Unadjusted	0.942 (0.905–0.980)	0.003
Adjusted (physicians, BMI, eGFR, lipid-lowering Tx)	0.951 (0.903–1.002)	0.061
European SCORE*BMI <25 kg/m^2		
Unadjusted	0.893 (0.837–0.952)	0.001
Adjusted (physicians, eGFR)	0.896 (0.833–0.964)	0.003
European SCORE*Glucose <126 mg/dL		
Unadjusted	0.974 (0.933–1.017)	0.236
Patients with previous stroke or MI		
European SCORE*DBP <90 mm Hg		
Unadjusted	0.784 (0.728–0.845)	<0.001
Adjusted (physicians, DM, BMI, eGFR, antihypertensive Tx)	0.746 (0.670–0.831)	<0.001
European SCORE*LDL-C < 130 mg/dL		

TABLE 3 (Continued)

Parameters	OR (95% CI)	*P* Value
Unadjusted	0.864 (0.785–0.911)	<0.001
Adjusted (physicians, DM, BMI, eGFR, lipid-lowering Tx)	0.849 (0.772–0.935)	0.001
European SCORE*HDL-C > 40 mg/dL (M) and > 50 mg/dL (F)		
Unadjusted	0.954 (0.890–1.023)	0.186
European SCORE*TG <160 mg/dL		
Unadjusted	0.851 (0.790–0.917)	<0.001
Adjusted (physicians, DM, BMI, eGFR, lipid-lowering Tx)	0.892 (0.811–0.981)	0.019
European SCORE*BMI <25 kg/m^2		
Unadjusted	0.944 (0.865–1.029)	0.192
European SCORE*Glucose <126 mg/dL		
Unadjusted	0.982 (0.919–1.050)	0.601

Abbreviations: BMI, body mass index; BP, blood pressure; CI, confidence interval; DBP, diastolic blood pressure; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; F, females; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; M, males; MI, myocardial infarction; OR, odds ratio; SCORE, Systematic Coronary Risk Evaluation; TG, triglycerides; Tx, treatment. In multivariate analyses the following covariates were considered, when appropriate: referring physicians, DM, BMI, BP, lipid- or glucose-lowering therapies, eGFR.

recommended therapeutic targets in their daily clinical practice. Also, poor control rates of CV risk factors cannot be related to the insufficient pharmacological and nonpharmacological therapies, because the higher the risk profile, the higher the proportions of patients who received educational advice and drug therapies (also in combined formulations). Many of the previous studies have supported a lesser control of risk factors in high-risk patients but associated with a similar proportion of treated patients supporting some degree of therapeutic inertia. This does not seem the case in the present study. Maybe the doses of drugs, the use of combinations, and the medication preferentially used represent some factors that may at least in part explain the apparent discrepancy between the higher rate of treatment and the lesser control of risk factors.

High SCORE risk estimations were an independent predictor of lower rates of control of all tested CV risk factors, not only systolic BP and TC (which are included in the risk equation), but also for additional risk factors, such as diastolic BP, LDL-C and HDL-C levels, TG, fasting glucose, and BMI (not included in the equation). These results were largely independent by the presence of pharmacological therapies and other covariates, including renal function and type of referring physician, and strongly support the use of the SCORE algorithm in a setting of real-world practice to help physicians for better identify high-risk individuals and implement preventive strategies for reducing the burden of CVD.

4.1 | Study limitations

The present study has some potential limitations that should be acknowledged.[15,16] First of all, it is based on a large, cross-sectional, descriptive survey. Second, dependence on physician self-reporting throughout predefined standardized questionnaires, rather than direct measures or quantifications of the tested variables, may create potential biases. Finally, patients included in the present analysis were consecutively enrolled about 10 years ago. During this time period, several sets of guidelines and recommendations from national and international societies have been produced, often proposing contrasting diagnostic thresholds and therapeutic targets for major CV risk factors and comorbidities. It should be noted, however, that BP targets were substantially unchanged over time, and that different LDL-C targets have been considered in the present analysis, thus being in line with current recommendations from international guidelines.

5 | CONCLUSION

In our analysis, we observed higher prevalence of uncontrolled major CV risk factors in adult outpatients with high SCORE risk profile. In these individuals, despite greater use of pharmacological drugs and recommendations for adopting favorable lifestyle measures, lower rates of control were observed, independently by referring physicians and other clinical characteristics. Further investigations should be performed to better identify potential causes of the observed relatively poor control rates of major risk factors to implement prevention of major CV outcomes in Italy.

Conflicts of interest

The authors declare no potential conflicts of interest.

ORCID

Massimo Volpe http://orcid.org/0000-0002-2395-7572
Giuliano Tocci http://orcid.org/0000-0002-0635-4921

REFERENCES

1. Rosengren A, Hawken S, Ounpuu S, et al; INTERHEART Investigators Association of psychosocial risk factors with risk of acute myocardial infarction in 11 119 cases and 13 648 controls from 52 countries (the INTERHEART study): case-control study *Lancet*. 2004;364:953–962.
2. Yusuf S, Hawken S, Ounpuu S, et al; INTERHEART InvestigatorsEffect of potentially modifiable risk factors associated with myocardial

infarction in 52 countries (the INTERHEART study): case-control study. *Lancet*. 2004;364:937–952.
3. Sakhuja A, Textor SC, Taler SJ. Uncontrolled hypertension by the 2014 evidence-based guideline: results from NHANES 2011–2012. *J Hypertens*. 2015;33:644–652.
4. Prugger C, Keil U, Wellmann J, et al; EUROASPIRE III Study Group. Blood pressure control and knowledge of target blood pressure in coronary patients across Europe: results from the EUROASPIRE III survey. *J Hypertens*. 2011;29:1641–1648.
5. Kotseva K, Wood D, De Backer G, et al; EUROASPIRE Study Group EUROASPIRE III: a survey on the lifestyle, risk factors and use of cardioprotective drug therapies in coronary patients from 22 European countries. *Eur J Cardiovasc Prev Rehabil*. 2009;16:121–137.
6. Halcox JP, Banegas JR, Roy C, et al. Prevalence and treatment of atherogenic dyslipidemia in the primary prevention of cardiovascular disease in Europe: EURIKA, a cross-sectional observational study. *BMC Cardiovasc Disord*. 2017;17:160.
7. Borghi C, Tubach F, De Backer G, et al. Lack of control of hypertension in primary cardiovascular disease prevention in Europe: results from the EURIKA study. *Int J Cardiol*. 2016;218:83–88.
8. Volpe M, Machado E. Treatment priorities and current prescribing patterns in hypertension: results of GRASP, an international physician survey. *Curr Med Res Opin*. 2004;20:1151–1160.
9. Volpe M, Tocci G. Managing hypertension in cardiology practice according to risk profile. *Int J Clin Pract*. 2008;62:1403–1412.
10. Graham I, Atar D, Borch-Johnsen K, et al. European guidelines on cardiovascular disease prevention in clinical practice: full text. Fourth Joint Task Force of the European Society of Cardiology and other societies on cardiovascular disease prevention in clinical practice (constituted by representatives of nine societies and by invited experts). *Eur J Cardiovasc Prev Rehabil*. 2007;14(suppl 2):S1–S113.
11. Piepoli MF, Hoes AW, Agewall S, et al. 2016 European Guidelines on cardiovascular disease prevention in clinical practice: the Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts)Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). *Eur Heart J*.2016;37:2315–2381.
12. Volpe M, Tocci G, Avogaro A, et al. Global cardiovascular risk assessment in different clinical settings: basal results of the EFFECTUS (Evaluation of Final Feasible Effect of Control Training and Ultra-Sensitisation) Programme. *High Blood Press Cardiovasc Prev*. 2009;16:55–63.
13. Tocci G, Ferrucci A, Guida P, et al. Global cardiovascular risk management in different Italian regions: an analysis of the Evaluation of Final Feasible Effect of Control Training and Ultra Sensitisation (EFFECTUS) educational program. *Nutr Metab Cardiovasc Dis*. 2012;22:635–642.
14. Tocci G, Ferrucci A, Guida P, et al. Use of electronic support for implementing global cardiovascular risk management: analysis of the results of the EFFECTUS (Evaluation of Final Feasible Effect of Control Training and Ultra Sensitisation) Educational Programme. *High Blood Press Cardiovasc Prev*. 2010;17:37–47.
15. Tocci G, Ferrucci A, Guida P, et al; EFFECTUS Steering Committee. Impact of diabetes mellitus on the clinical management of global cardiovascular risk: analysis of the results of the Evaluation of Final Feasible Effect of Control Training and Ultra Sensitization (EFFECTUS) educational program. *Clin Cardiol*. 2011;34:560–566.
16. Tocci G, Battistoni A, D'Agostino M, et al. Impact of hypertension on global cardiovascular risk stratification: analysis of a large cohort of outpatient population in Italy. *Clin Cardiol*. 2015;38:39–47.
17. Mancia G, Fagard R, Narkiewicz K, et al. 2013 ESH/ESC guidelines for the management of arterial hypertension: the Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *Eur Heart J*. 2013;34:2159–2219.
18. Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults. Executive summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA*. 2001;285:2486–2497.
19. Sesti G, Volpe M, Cosentino F, et al. Metabolic syndrome: diagnosis and clinical management, an official document of the *Working Group of the Italian Society of Cardiovascular Prevention (SIPREC). High Blood Press Cardiovasc Prev*. 2006;13:185–198.
20. Grundy SM, Brewer HB Jr, Cleeman JI, et al. Definition of metabolic syndrome: report of the National Heart, Lung, and Blood Institute/American Heart Association conference on scientific issues related to definition. *Circulation*. 2004;109:433–438.
21. Grundy SM, Cleeman JI, Daniels SR, et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. *Circulation*. 2005;112:2735–2752.
22. Rydén L, Standl E, Bartnik M, et al. Guidelines on diabetes, pre-diabetes, and cardiovascular diseases: executive summary. The Task Force on Diabetes and Cardiovascular Diseases of the European Society of Cardiology (ESC) and of the European Association for the Study of Diabetes (EASD). *Eur Heart J*. 2007;28:88–136.
23. American Diabetes Association Diagnosis and classification of diabetes mellitus. *Diabetes Care*. 2010;33(suppl 1):S62–S69.
24. Volpe M, Borghi C, Cavallo Perin P, et al. Cardiovascular prevention in subjects with impaired fasting glucose or impaired glucose tolerance. *High Blood Press Cardiovasc Prev*. 2010;17:73–102.
25. Van de Werf F, Bax J, Betriu A, et al. Management of acute myocardial infarction in patients presenting with persistent ST-segment elevation: the Task Force on the Management of ST-Segment Elevation Acute Myocardial Infarction of the European Society of Cardiology. *Eur Heart J*. 2008;29:2909–2945.
26. Bassand JP, Hamm CW, Ardissino D, et al. Guidelines for the diagnosis and treatment of non–ST-segment elevation acute coronary syndromes. *Eur Heart J*. 2007;28:1598–1660.
27. Thygesen K, Alpert JS, White HD; Joint ESC/ACCF/AHA/WHF Task Force for the Redefinition of Myocardial Infarction. Universal definition of myocardial infarction. *Eur Heart J*. 2007;28:2525–2538.
28. Goldstein LB, Adams R, Alberts MJ, et al. Primary prevention of ischemic stroke: a guideline from the American Heart Association/American Stroke Association Stroke Council: cosponsored by the Atherosclerotic Peripheral Vascular Disease Interdisciplinary Working Group; Cardiovascular Nursing Council; Clinical Cardiology Council; Nutrition, Physical Activity, and Metabolism Council; and the Quality of Care and Outcomes Research Interdisciplinary Working Group: the American Academy of Neurology affirms the value of this guideline [published correction appears in *Stroke*. 2007;38:207]. *Stroke*. 2006;37:1583–1633.
29. Easton JD, Saver JL, Albers GW, et al. Definition and evaluation of transient ischemic attack: a scientific statement for healthcare professionals from the American Heart Association/American Stroke Association Stroke Council; Council on Cardiovascular Surgery and Anesthesia; Council on Cardiovascular Radiology and Intervention; Council on Cardiovascular Nursing; and the Interdisciplinary Council on Peripheral Vascular Disease. The American Academy of Neurology affirms the value of this statement as an educational tool for neurologists. *Stroke*. 2009;40:2276–2293.
30. Conroy RM, Pyörälä K, Fitzgerald AP, et al; SCORE Project Group. Estimation of 10-year risk of fatal cardiovascular disease in Europe: the SCORE project. *Eur Heart J*. 2003;24:987–1003.
31. Tocci G, Ferrucci A, Pontremoli R, et al. Blood pressure levels and control in Italy: comprehensive analysis of clinical data from 2000–2005 and 2005–2011 hypertension surveys. *J Hum Hypertens*. 2015;29:696–701.
32. Tocci G, Nati G, Cricelli C, et al. Prevalence and control of hypertension in the general practice in Italy: updated analysis of a large database. *J Hum Hypertens*. 2017;31:258–262.
33. Banegas JR, López-García E, Dallongeville J, et al. Achievement of treatment goals for primary prevention of cardiovascular disease in clinical practice across Europe: the EURIKA study. *Eur Heart J*. 2011;32:2143–2152.
34. Whyte JL, Lapuerta P, L'Italien GJ, et al. The challenge of controlling systolic blood pressure: data from the National Health and Nutrition

Examination Survey (NHANES III), 1988–1994 *[published correction appears in J Clin Hypertens (Greenwich). 2002;4:76]. J Clin Hypertens (Greenwich)*. 2001;3:211–216.

How to cite this article: Figliuzzi I, Presta V, Citoni B, et al. Achievement of multiple therapeutic targets for cardiovascular disease prevention: Retrospective analysis of real practice in Italy. *Clin Cardiol*. 2018;41:788–796. https://doi.org/10.1002/clc.22955