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Atherosclerosis xxx (2006) xxx–xxx

www.elsevier.com/locate/atherosclerosis

ATHEROSCLEROSIS

Unmet needs in the diagnosis and treatment of dyslipidemia in the primary care setting in Germany

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Received 4 November 2005; received in revised form 26 January 2006; accepted 2 February 2006

Abstract

Objectives and methods: DETECT is a cross-sectional study of 55,518 unselected consecutive patients in 3188 representative primary care offices in Germany. In a random subset of 7519 patients, an extensive standardized laboratory program was undertaken. The study investigated the prevalence of cardiovascular disease, known risk factors (such as diabetes, hypertension and dyslipidemia and their co-morbid manifestation), as well as treatment patterns. The present analysis of the DETECT laboratory dataset focused on the prevalence and treatment of dyslipidemia in primary medical care in Germany. Coronary artery disease (CAD), risk categories and LDL-C target achievement rates were determined in the subset of 6815 patients according to the National Cholesterol Education Program (NCEP) ATP III Guidelines.

Results: Of all patients, 54.3% had dyslipidemia. Only 54.4% of the NCEP-classified dyslipidemic patients were diagnosed as 'dyslipidemic' by their physicians. Only 27% of all dyslipidemic patients (and 40.7% of the recognized dyslipidemic patients) were treated with lipid-lowering medications, and 11.1% of all dyslipidemic patients (41.4% of the patients treated with lipid-lowering drugs) achieved their LDL-C treatment goals. In conclusion, 80.3% of patients in the sample with dyslipidemia went undiagnosed, un-treated or under-treated.

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Keywords: Dyslipidemia; Cardiovascular risk; Coronary heart disease; Lipid disorders; Risk factors; Prevalence

1. Introduction

A recent evaluation of the Framingham and the Third National Health and nutrition examination survey (NHANES III) datasets revealed that more than 90% of coronary artery disease (CAD) events occurs in individuals with at least one of the five major CAD risk factors: hypertension, elevated low-

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density lipoproteins, low high-density lipoproteins, glucose intolerance and smoking [1]. Dyslipidemia thus is among the key risk factors for the development of cardiovascular disease.

Despite minor differences in the definition of dyslipidemia and the goals of treatment between the major guidelines, the targets are being lowered for total cholesterol (TC) and LDL-cholesterol (LDL-C). Recently, the European guidelines on cardiovascular disease prevention in clinical practice recommended a TC of below 190 mg/dl (5.0 mmol/l) and a LDL-C of below 115 mg/dl (3.0 mmol/l) for the general population. In dependence of the total cardiovascular risk and treatment success only lifestyle therapy or additional drug treatment is recommended. In patients with clinically established coronary artery disease (CAD), other cardiovascular diseases (CVD) or diabetes mellitus the recommended goals are even lower: TC <175 mg/dl (4.5 mmol/l) and LDL-C <100 mg/dl (2.6 mmol/l) [2]. The current National Cholesterol Education Program (NCEP) guidelines recommend the following LDL-C levels: <160 mg/dl (4.1 mmol/l) in subjects with zero to one risk factors; <130 mg/dl (3.4 mmol/l) in subjects with two or more risk factors and a 10-year risk for hard CAD (myocardial infarction or CAD death) less than 20%; <100 mg/dl (2.6 mmol/l) in patients with CAD or CAD equivalents such as diabetes mellitus or a 10 year-risk for CAD greater than 20% [3]. In the UK, the LDL-C goals for patients at risk are even lower (British Hypertension Society guidelines) [4]. The NCEP coordination committee, encouraged by the results of recent major statin trials, recommended a goal for LDL-C of less than 70 mg/dl (1.8 mmol/l) in patients at very high risk, at least as a therapeutic option [5]. We expect these therapeutic options to be changed into guidelines as soon as the results of two large outcome studies are available. One is the treating to new targets (TNT) study, which has already been published. It revealed that a further decrease in the LDL-C blood level from 101 mg/dl (2.6 mmol/l) to 77 mg/dl (2.0 mmol/l), achieved with a higher statin dosage (80 mg atorvastatin versus 10 mg atorvastatin) significantly lowered the relative risk for the combined cardiovascular endpoint by 22% (absolute risk reduction 2.2%, NNT 46) [6,7]. The second study is the incremental decrease in end points through aggressive lipid-lowering (IDEAL) study. This study compares conventional-dose statin therapy (20 or 40 mg simvastatin) with a more aggressive regimen (80 mg atorvastatin). It thus addresses the question whether achievement of LDL-C levels below 70 mg/dl translates into a continuing reduction of cardiovascular risk [8].

In sharp contrast to the increasing awareness and stricter cut-offs in the European and US American guidelines for the treatment of dyslipidemia, comparatively little is known about the actual situation in the setting for which most of those guidelines have been developed, namely the primary care sector. For example, in Germany only limited data on the prevalence and the distribution of risk factors are available. Most surveys have examined the prevalence and treatment patterns in patients at risk [9] or in a regionally

clustered fashion such as PROCAM or MONICA or others [10–16], and many are partly out of date [8–14]. Against the background of the rapidly changing guidelines and treatment environment, a remarkable need exists for comprehensive data from large studies on the prevalence of dyslipidemia, its recognition and control in primary care practice. This need prompted us to initiate a nationally representative large-scale epidemiological study (DETECT) [17,18] to assess the prevalence of dyslipidemia, other cardiovascular risk factors, and dyslipidemia management patterns in primary care.

In this paper we examine: (1) the point prevalence of treated and untreated dyslipidemia in primary care; (2) modalities and efficacy of treatment; (3) associations between dyslipidemia and CVD.

2. Methods

2.1. Design

DETECT is a large, multistage cross-sectional study of 55,518 unselected consecutive patients (59% women; mean age 53.9 years) in 3188 primary care offices in Germany (73% general medicine and 27% internal medicine) with a prospective 12-month component in a random subset of 7519 patients, characterized additionally by an extensive standardized laboratory program with focus on CV risk assessment. Patient self-assessment and physician assessment were obtained for each patient. Further details are available at <http://www.detect-studie.de>. The rationale and design for DETECT, baseline characteristics and preliminary prevalence data have been published by Wittchen and Böhler et al. [17,18]. In 7376 out of the random subset of 7519 patients complete lipid and lipoprotein analyses were performed. Due to the lower and upper age boundaries of the Framingham risk score tables, Framingham risk scores were calculated only in the subset of 6815 patients within the age range of 20–79 years. A comparison of the sub-sample of 6815 patients to the total sample of 7519 patients revealed no relevant differences for age, sex, clinical diagnosis, BMI, smoking and alcohol consumption between both groups.

2.2. CAD risk categories, dyslipidemia and diabetes definitions

CAD risk categories and subsequent LDL-C goals were determined according to the National Cholesterol Education Program (NCEP) ATP III Guidelines (Table 1). Ten-year risk for hard CAD (MI and CAD death) was calculated according to the Framingham risk score. Dyslipidemia was diagnosed if LDL-C levels exceeded the target values demanded by the NCEP risk classes I–III, or if there was a clinical history of dyslipidemia (physician diagnosis or a prescription for lipid-lowering medication). The risk classes were defined as follows. NCEP risk class I: 0 or 1 risk factor; NCEP risk class II: 2 or more risk factors, or 10 year

Table 1
LDL^a cholesterol goals and cutpoints for therapeutic lifestyle changes (TLC) and drug therapy in the different risk categories

Risk category	LDL goal (mg/dl)	LDL level at which to initiate therapeutic lifestyle changes (mg/dl)	LDL level at which to consider drug therapy (mg/dl)
CHD or CHD risk equivalents ^c (10-year risk >20%)	<100	≥100	≥130 (100–129: drug optional) ^b
>2 Risk factors (10-year risk ≤20%)	<130	≥130	10-year risk 10–20%: ≥130 10-year risk <10%: ≥160
0–1 Risk factor ^d	<160	≥160	≥190 (160–189: LDL-lowering drug optional)

^a LDL indicates low-density lipoprotein; CHD, coronary heart disease.

^b Some authorities recommend use of LDL-lowering drugs in this category if an LDL cholesterol level of <100 mg/dl cannot be achieved by therapeutic lifestyle changes. Others prefer use of drugs that primarily modify triglycerides and HDL, e.g. Nicotinic acid or fibrate. Clinical judgment also may call for deferring drug therapy in this subcategory.

^c CHD risk equivalents comprise:

- other clinical forms of atherosclerotic disease (peripheral arterial disease, abdominal aortic aneurysm and symptomatic carotid artery disease);
- diabetes;
- multiple risk factors that confer a 10-year risk for CHD > 20%.

^d Almost all people with 0–1 risk factor have a 10-year risk <10%; thus, 10-year risk assessment in people with 0–1 risk factor is not necessary.

risk ≤20%; NCEP risk class III: 10 year risk >20% or a diagnosis of CAD or previous stroke or symptomatic carotid stenosis or peripheral arterial disease (PAD). NCEP risk factors included: cigarette smoking, hypertension (BP ≥140/90 mmHg or a prescription for antihypertensive medication), low HDL cholesterol (<40 mg/dL), family history of premature CAD (CAD in male first-degree relative <55 years; CAD in female first-degree relative <65 years), age (men ≥45 years; women ≥55 years) [3]. Due to a recent publication by Hense et al. [19], which reported an overprediction of the CV risk in Germany by using the Framingham score, we additionally performed the PROCAM risk calculation for dyslipidemia prevalence estimations as well.

Diabetes was defined according to the guidelines of the American Diabetes Association (fasting plasma glucose >126 mg/dl, no caloric intake for at least 8 h) or clinical history (physician diagnosis or prescription for an antidiabetic medication).

2.3. Blood pressure measurements

Blood pressure measurements were performed according to the guidelines of the German Hypertension Society.

2.4. Lipids and lipoproteins

Fasting blood samples were collected and shipped by courier within 24 h to the central laboratory at the Medical University of Graz (Austria). Clinical chemical parameters as well as cholesterol, triglycerides and lipoprotein (a) [Lp(a)] were determined on a Roche Modular automatic analyser. Lipoproteins (HDL, LDL and VLDL) were determined electrophoretically on the HELENA SAS-3/SAS-4 system. Haemoglobin (Hb) A1c was determined chromatographically on an ADAMS HA 8160 analysing system. For all parameters, reagents and secondary standards were used as recommended by the manufacturers.

2.5. Statistical analyses

Prevalence estimates were based on the assessment of the laboratory subset of unselected consecutive primary care attendees in the participating centers on the study day and are thus point prevalence estimates. The data were weighted to adjust for non-response and differences in the laboratory sampling process between the laboratory sample and the main study sample. Using cross tables, frequency distributions and descriptive statistics, we compared the distributions of variables among all categories. All statistical analyses were conducted with the software package STATA 8 [20].

3. Results

3.1. Patient population

A total of 4086 patients (54.3%) out of the 6815 patients with complete Framingham risk classification were identified as dyslipidemic by the criteria of the NCEP ATP III guidelines. Only 1170 patients received lipid-lowering medication (27% of all patients with dyslipidemia).

Among those with dyslipidemia, patients treated with lipid-lowering (LL) drugs were older, smoked less, had a lower total cholesterol, a lower LDL-cholesterol and slightly higher levels of triglycerides than those not receiving LL drugs. In the latter, more patients had HbA1c serum levels over 6.5% and more patients with fasting plasma glucose levels over 126 mg/dl. The rates of overweight and obese patients, the amount of alcohol consumed, serum creatinine levels and blood pressure and heart rate were comparable between groups. Based on physician diagnosis, the medically treated group had significantly higher rates of patients with metabolic and cardiovascular diseases such as diabetes, hypertension, myocardial infarction, stroke

and atherosclerotic diseases (CAD or carotid stenosis or PAD). Interestingly, only 45.4% of the dyslipidemic patients without lipid-lowering treatment were classified by their physicians as being dyslipidemic compared to 82.0% in the group treated with lipid-lowering compounds.

Table 2 summarizes the demographic characteristics and medical history of the total sample ($n = 6815$), the group of patients with NCEP dyslipidemia, and the groups of medically untreated and treated patients.

3.2. NCEP risk classification

Of the patients with NCEP dyslipidemia, 20.8% were classified as NCEP risk class I, and 27% as NCEP risk class II with no major difference in gender, 52.2% were classified as NCEP risk class III with a higher portion of men. The age distribution of dyslipidemia shows a continuous increase with age; the majority of patients with NCEP dyslipidemia are over 50 years old. Only 0.5% of the dyslipidemic patients

Table 2
Patient characteristics and medical history

	Total sample ($N = 6815$) N (%)	Total dyslipidemia ($N = 4086$) N (%)	Dyslipidemia, without lipid-lowering drugs ($N = 2916$) N (%)	Dyslipidemia, treated with lipid-lowering drugs ($N = 1170$) N (%)
Patients' characteristics				
Total	6815 (100)	4086 (54.3)	2843 (73.0)	1170 (27.0)
Sex				
Female	3978 (59.5)	2125 (51.8)	1597 (54.6)	528 (44.6)
Male	2837 (40.5)	1961 (48.2)	1319 (45.4)	642 (55.4)
Age (years)				
<=60	3730 (58.2)	1664 (42.4)	1289 (46.3)	375 (32.2)
>60	3085 (41.8)	2422 (57.6)	1627 (53.7)	795 (67.9)
Body mass category				
Overweight	2702 (39.1)	1769 (43.6)	1244 (43.0)	525 (45.4)
Obesity	1666 (22.5)	1239 (29.3)	876 (29.1)	363 (29.9)
Smoking status				
Present	1457 (22.2)	824 (21.2)	643 (23.3)	181 (15.7)
Past	1632 (23.2)	1091 (25.9)	710 (23.5)	381 (32.5)
Alcohol consumption				
Sometimes	4669 (69.3)	2675 (65.9)	1928 (66.6)	747 (64.0)
Often	823 (11.7)	549 (13.3)	381 (12.9)	168 (14.3)
HbA1c > 6.5%	627 (7.6)	572 (12.6)	375 (11.4)	197 (15.9)
Fasting plasma glucose >126 mg/dl	948 (11.9)	847 (19.3)	559 (17.8)	288 (23.2)
Systolic BP ^a (mmHg)	132.3 (18.56)	136.4 (18.23)	136.3 (18.44)	136.8 (17.69)
Diastolic BP ^a (mmHg)	80.2 (10.03)	81.5 (9.91)	81.8 (9.96)	80.8 (9.77)
Heart rate ^a (bpm)	72.8 (10.41)	72.7 (10.32)	72.9 (10.29)	72 (10.38)
Total cholesterol ^a (mg/dl)	223.6 (43.13)	237 (43.99)	243.3 (39.53)	221 (50.1)
HDL cholesterol ^a (mg/dl)	54.5 (18.69)	50.9 (17.61)	51.6 (17.71)	49.2 (17.26)
LDL cholesterol ^a (mg/dl)	127.6 (33.83)	139.5 (34.18)	145.9 (30.6)	123.5 (37.26)
Triglycerides ^a (mg/dl)	155.4 (132.57)	179.9 (150.51)	170.6 (113.7)	202.9 (214.88)
Lipoprotein (a) ^a	33.1 (44.1)	36.2 (47.89)	33.6 (43.36)	42.7 (57.2)
Creatinine ^a (mg/dl)	1.2 (0.26)	1.2 (0.28)	1.2 (0.25)	1.3 (0.34)
Medical history				
Hyperlipidemia	2387 (29.5)	2387 (55.5)	1411 (45.4)	976 (82.0)
Diabetes mellitus type 2	1151 (13.7)	1052 (23.4)	668 (20.7)	384 (30.6)
Hypertension	2721 (34.6)	2186 (50.2)	1402 (44.6)	784 (65.2)
LVH ^b	389 (4.9)	335 (7.7)	183 (5.7)	152 (12.8)
CAD ^c	863 (11.0)	795 (17.7)	353 (10.0)	442 (37.9)
MI ^d	326 (4.2)	306 (7.1)	92 (2.8)	214 (18.6)
Carotid stenosis	109 (1.4)	99 (2.2)	27 (0.8)	72 (6.0)
Stroke	234 (3.1)	222 (4.9)	122 (3.6)	100 (8.5)
PAD ^e	223 (2.8)	205 (4.6)	96 (2.8)	109 (9.2)
Atherosclerotic disease (CAD or carotid stenosis or PAD)	1016 (13.0)	932 (20.7)	432 (12.3)	500 (42.7)

^a Data shown as mean (S.D.).

^b LVH: left ventricular hypertrophy.

^c CAD: coronary artery disease.

^d MI: myocardial infarction.

^e PAD: peripheral artery disease.

Table 3
Age and sex-dependent rates of dyslipidemia by NCEP risk class

	Total N (%)	20–29 years N (%)	30–39 years N (%)	40–49 years N (%)	50–59 years N (%)	60–69 years N (%)	70–79 years N (%)
Total	4086 (100.0)	22 (0.5)	183 (4.5)	523 (12.8)	828 (20.3)	1447 (35.4)	1083 (26.5)
NCEP risk class I	823 (20.8)	9 (42.1)	77 (40.7)	189 (36.1)	190 (23.7)	235 (16.8)	123 (11.6)
NCEP risk class II	1040 (27.0)	9 (42.6)	58 (34.4)	164 (32.7)	269 (33.7)	390 (28.7)	150 (14.8)
NCEP risk class III	2223 (52.2)	4 (15.4)	48 (25.0)	170 (31.2)	369 (42.6)	822 (54.5)	810 (73.6)
Female	2125 (100.0)	12 (0.6)	87 (4.3)	247 (12.3)	408 (19.6)	752 (34.8)	619 (28.3)
NCEP risk class I	607 (29.4)	5 (41.7)	42 (46.2)	127 (51.4)	152 (37.9)	182 (25.0)	99 (16.4)
NCEP risk class II	578 (28.7)	4 (36.6)	28 (35.9)	62 (25.9)	127 (32.1)	245 (34.1)	112 (19.6)
NCEP risk class III	940 (42.0)	3 (21.7)	17 (17.9)	58 (22.8)	129 (30.0)	325 (40.9)	408 (64.1)
Male	1961 (100.0)	10 (0.6)	96 (5.2)	276 (14.9)	420 (21.6)	695 (34.5)	464 (23.1)
NCEP risk class I	216 (11.6)	4 (42.5)	35 (35.7)	62 (22.6)	38 (9.8)	53 (7.9)	24 (5.3)
NCEP risk class II	462 (25.3)	5 (49.2)	30 (33.0)	102 (38.7)	142 (35.3)	145 (22.8)	38 (8.6)
NCEP risk class III	1283 (63.2)	1 (8.3)	31 (31.3)	112 (38.7)	240 (54.9)	497 (69.3)	402 (86.2)

were younger than 30 years, mostly classified as NCEP risk class I or II.

In the group between 20 and 29 years of age, 15.4% of patients were within NCEP risk class III. The proportion of patients within NCEP risk class III continuously increased with age and represented the majority of patients in the age group between 50 and 59 years. In the age group between 70 and 79 years, most patients were classified as NCEP risk class III (86.2%). Men were more frequently classified as NCEP risk class III compared to women and achieved this NCEP risk class at an earlier age. Table 3 and Fig. 1 lists the age and sex dependent rates by ATP III NCEP risk classes I–III.

3.3. Assignment of dyslipidemia diagnoses

Only 2387 (54.4%) of the 4086 NCEP dyslipidemic patients were diagnosed as ‘dyslipidemic’ by their physicians, with no major gender differences. The frequency of being diagnosed as dyslipidemic increased with age, ranging from 22.8% in patients in the age group 20–29 years to nearly 60% in the age group 60–69 years (Table 4a). The rate of diagnosed dyslipidemia was higher in NCEP risk classes

I and III compared to NCEP risk class II (61.5% and 57.4%, respectively versus 43%).

3.4. Treatment rates

A total of 1170 (27%) (Table 4a) of the NCEP dyslipidemic patients and 976 (40.7%) (Table 4b) of the recognized dyslipidemic patients were treated with lipid-lowering medication. The majority of the recognized patients received additional lifestyle interventions (70%) with a higher rate in men than women, which significantly increased with age (Table 4b). Especially in NCEP risk class I, significantly more men than women received lipid-lowering treatment (26% versus 16.3% and 35.9% versus 20.2% in the recognized patients) mostly in the age group between 30 and 59 years. In NCEP risk classes II and III, no major gender or age-related differences were observed, except for an approximately 10% higher rate of lipid-lowering treatment in men compared to women in the NCEP risk class III, across the age groups from 40 to 69 years.

3.5. LDL-C goal achievement

Only 41.4% of patients treated with lipid-lowering drugs were at their target level for LDL-C (11.1% of all dyslipidemic patients, respectively). Men achieved their goals more frequently than women (Table 4a). In NCEP risk class I, significantly more patients achieved their target level than did those in NCEP risk classes II and III (13.2% versus 8.6% and 11.7%, respectively).

A total of 10.8% of all patients achieved their NCEP LDL-C goal without any lipid-lowering treatment. Most of these patients were in the age group between 20 and 49 years, and women achieved their goals without treatment more frequently than men (Table 4a). This effect can be found throughout all NCEP risk classes. The proportion of these patients was higher within NCEP risk class I (31.6%) compared to NCEP risk classes II and III (8.7%

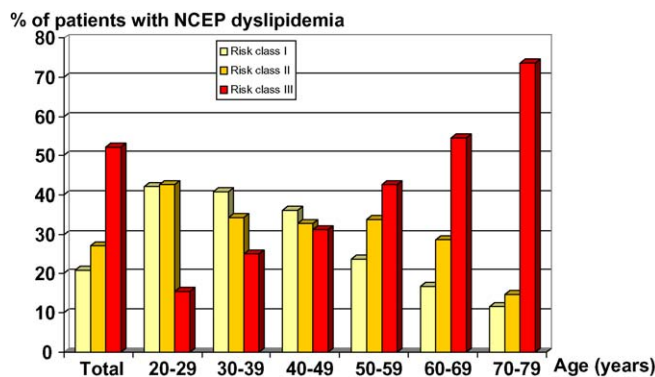


Fig. 1. Age-dependent rates of dyslipidemia by NCEP risk class.

Table 4a

Rates for clinically diagnosed dyslipidemia, patients with lipid-lowering drug treatment, goal attainment and patients achieving their goals without drug treatment

		Clinicians diagnosis N (%)	Lipid-lowering treatment ^a N (%)	At goal with LL treatment N (%)	At goal without LL treatment N (%)
Total	4086	2387 (54.4)	1170 (27.0)	484 (11.1)	471 (10.8)
20–29	22	6 (22.8)	2 (7.3)	0 (0.0)	4 (15.4)
30–39	183	96 (46.1)	22 (10.2)	13 (6.1)	38 (18.3)
40–49	523	265 (44.7)	94 (16.4)	42 (7.3)	93 (15.7)
50–59	828	486 (54.1)	223 (25.0)	96 (10.8)	88 (9.9)
60–69	1447	869 (56.8)	452 (29.9)	184 (12.1)	157 (10.4)
70–79	1083	665 (58.8)	377 (33.9)	149 (13.3)	91 (8.1)
Female	2125	1267 (55.6)	528 (23.3)	217 (9.7)	300 (13.4)
20–29	12	3 (21.1)	2 (13.9)	0 (0.0)	1 (7.0)
30–39	87	49 (50.0)	4 (3.6)	2 (1.7)	21 (21.4)
40–49	247	127 (45.1)	29 (10.5)	15 (5.4)	63 (22.7)
50–59	408	246 (55.9)	76 (16.9)	35 (7.8)	62 (14.2)
60–69	752	452 (56.8)	199 (25.2)	81 (10.5)	94 (12.1)
70–79	619	390 (60.0)	218 (34.1)	84 (13.3)	59 (9.3)
Male	1961	1120 (53.1)	642 (31.0)	267 (12.7)	171 (8.1)
20–29	10	3 (24.8)	0 (0.0)	0 (0.0)	3 (24.8)
30–39	96	47 (42.6)	18 (16.0)	11 (10.1)	17 (15.5)
40–49	276	138 (44.3)	65 (21.6)	27 (9.0)	30 (9.5)
50–59	420	240 (52.4)	147 (32.9)	61 (13.7)	26 (5.6)
60–69	695	417 (56.8)	253 (35.0)	103 (14.0)	63 (8.6)
70–79	464	275 (57.3)	159 (33.7)	65 (13.3)	32 (6.5)

^a N = 150 patients treated with lipid-lowering medication but not recognized by clinician.

and 3.6%, respectively). Table 4a and Fig. 2 summarize the categories and age and sex-dependent rates of dyslipidemia diagnosis, lipid-lowering treatment and goal achievement for LDL-C, Table 4b summarizes the rates and types of lipid-lowering intervention for patients with clinically diagnosed dyslipidemia.

3.6. Under-recognition and under-treatment of dyslipidemia

Of all patients with NCEP dyslipidemia, 45.6% have not been identified by their treating physician as dyslipidemic; 21.4% have been recognized but not treated with lipid-

Table 4b

Rates and types of interventions for patients with clinically diagnosed dyslipidemia

	Clinicians diagnosis (n = 2387) N	Only lipid-lowering treatment (n = 271) N (%)	Only Lifestyle intervention (n = 974) N (%)	Both interventions (n = 705) N (%)	Any intervention (n = 1950) N (%)	Any lipid-lowering treatment (n = 976) N (%)
Total	2387	271 (11.5)	974 (40.8)	705 (29.2)	1950 (81.5)	976 (40.7)
20–29	6	0 (0.0)	4 (67.5)	1 (16.3)	5 (83.8)	1 (16.3)
30–39	96	5 (5.1)	59 (61.9)	15 (15.2)	79 (82.2)	20 (20.3)
40–49	265	11 (4.1)	126 (47.1)	68 (26.0)	205 (77.2)	79 (30.1)
50–59	486	50 (10.4)	207 (42.7)	139 (28.2)	396 (81.3)	189 (38.6)
60–69	869	105 (12.1)	355 (40.9)	267 (30.4)	727 (83.4)	372 (42.5)
70–79	665	100 (15.5)	223 (33.4)	215 (31.9)	538 (80.8)	315 (47.4)
Female	1267	118 (9.3)	563 (44.6)	327 (25.3)	1008 (79.2)	445 (34.6)
20–29	3	0 (0.0)	1 (33.3)	1 (33.3)	2 (66.7)	1 (33.3)
30–39	49	1 (1.8)	35 (71.5)	2 (4.1)	38 (77.5)	3 (5.9)
40–49	127	3 (2.4)	66 (51.8)	23 (17.8)	92 (72.0)	26 (20.2)
50–59	246	15 (6.2)	111 (45.5)	54 (21.1)	180 (72.8)	69 (27.3)
60–69	452	40 (8.7)	210 (46.7)	124 (27.1)	374 (82.4)	164 (35.8)
70–79	390	59 (15.4)	140 (35.9)	123 (31.0)	322 (82.3)	182 (46.4)
Male	1120	153 (13.9)	411 (36.5)	378 (33.6)	942 (84.0)	531 (47.6)
20–29	3	0 (0.0)	3 (100.0)	0 (0.0)	3 (100.0)	0 (0.0)
30–39	47	4 (8.6)	24 (51.7)	13 (26.8)	41 (87.1)	17 (35.4)
40–49	138	8 (5.7)	60 (42.8)	45 (33.3)	113 (81.8)	53 (39.0)
50–59	240	35 (14.8)	96 (39.8)	85 (35.5)	216 (90.1)	120 (50.3)
60–69	417	65 (15.8)	145 (34.6)	143 (34.0)	353 (84.4)	208 (49.8)
70–79	275	41 (15.5)	83 (29.9)	92 (33.2)	216 (78.6)	133 (48.7)

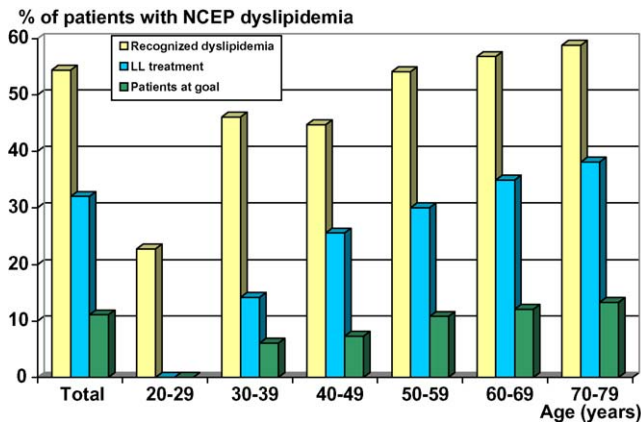


Fig. 2. Age-dependent rates for diagnosis, treatment and goal achievement of clinically diagnosed dyslipidemia.

lowering drugs; 13.2% have been recognized and treated but have not achieved their treatment goals. Dyslipidemia in the elderly was unrecognized less frequently; however, these patients were more frequently under-treated and showed significantly lower goal achievement rates compared to younger patients. The recognition rates were significantly better in patients with MI and PAD and only slightly better in patients with stroke, hypertension and diabetes mellitus. The treatment rates were better in patients with MI and stroke (only 13.6% and 20.9% of the patients were recognized but not treated with lipid-lowering drugs compared to 21.4% overall). Goal achievement was worse in patients with CV diseases or in patients at high risk. The rates of treated patients not at goal were worse in patients with MI, PAD, stroke, hypertension and diabetes mellitus. Table 5 shows age-dependent rates for under-recognition, under-treatment and under-achievement of goals for dyslipidemia in all patients with NCEP dyslipidemia and subgroups with CV diseases and distinct CV risk factors.

Table 5

Age-dependent under-recognition and under-treatment of dyslipidemia in distinct CV disease and CV risk factor groups

	Total N (%)	20–29 years N (%)	30–39 years N (%)	40–49 years N (%)	50–59 years N (%)	60–69 years N (%)	70–79 years N (%)
Total	4086 (100.0)	22 (0.6)	183 (4.8)	523 (13.6)	828 (20.6)	1447 (34.7)	1083 (25.8)
NR	1699 (45.6)	16 (77.2)	87 (53.9)	258 (55.3)	342 (45.9)	578 (43.2)	418 (41.2)
RNT	940 (21.4)	1 (3.7)	38 (18.5)	93 (15.6)	209 (23.4)	340 (22.2)	259 (22.9)
RTNG	579 (13.2)	1 (3.7)	9 (4.0)	43 (7.3)	109 (12.1)	222 (14.4)	195 (17.5)
MI	306 (100.0)	0 (0.0)	0 (0.0)	21 (7.0)	48 (15.4)	114 (36.3)	123 (41.3)
NR	72 (24.7)	0 (0.0)	0 (0.0)	4 (21.8)	10 (22.2)	27 (24.1)	31 (26.7)
RNT	43 (13.6)	0 (0.0)	0 (0.0)	5 (20.3)	7 (14.8)	15 (12.8)	16 (12.8)
RTNG	91 (30.2)	0 (0.0)	0 (0.0)	4 (18.7)	17 (35.0)	30 (27.1)	40 (33.0)
Stroke	222 (100.0)	0 (0.0)	4 (1.9)	7 (3.8)	30 (13.1)	85 (37.3)	96 (43.9)
NR	82 (40.4)	0 (0.0)	1 (32.8)	4 (67.5)	9 (36.4)	30 (37.6)	38 (41.9)
RNT	49 (20.9)	0 (0.0)	3 (67.3)	1 (12.7)	5 (15.9)	20 (22.5)	20 (19.7)
RTNG	54 (23.4)	0 (0.0)	0 (0.0)	2 (19.9)	7 (22.4)	23 (26.1)	22 (22.8)
PAD	205 (100.0)	0 (0.0)	0 (0.0)	4 (2.2)	27 (12.5)	83 (40.6)	91 (44.7)
NR	56 (29.5)	0 (0.0)	0 (0.0)	2 (51.9)	8 (29.8)	23 (29.9)	23 (27.9)
RNT	50 (23.4)	0 (0.0)	0 (0.0)	1 (24.5)	9 (32.1)	14 (16.4)	26 (27.2)
RTNG	52 (25.2)	0 (0.0)	0 (0.0)	1 (23.6)	6 (23.5)	25 (29.4)	20 (21.9)
Overweight	1791 (100.0)	1 (0.1)	61 (3.6)	215 (12.9)	349 (20.1)	661 (36.3)	504 (27.1)
NR	766 (46.7)	1 (100.0)	29 (53.8)	115 (59.3)	143 (46.1)	279 (45.4)	199 (41.7)
RNT	408 (21.3)	0 (0.0)	10 (14.6)	37 (15.1)	85 (22.3)	159 (22.9)	117 (22.4)
RTNG	265 (13.8)	0 (0.0)	4 (5.6)	20 (8.0)	48 (12.6)	96 (13.6)	97 (18.8)
Obesity	1248 (100.0)	8 (0.7)	54 (4.7)	152 (12.7)	261 (20.9)	472 (36.9)	301 (24.2)
NR	487 (42.2)	5 (63.9)	22 (47.2)	65 (47.3)	102 (42.1)	179 (40.4)	114 (40.7)
RNT	326 (24.8)	1 (11.5)	18 (30.5)	33 (19.9)	71 (26.0)	123 (25.1)	80 (25.3)
RTNG	184 (13.9)	1 (11.5)	3 (4.1)	12 (7.3)	40 (14.4)	79 (15.9)	49 (16.0)
Hypertension	2186 (100.0)	3 (0.1)	36 (1.7)	142 (6.7)	382 (17.5)	885 (40.4)	738 (33.6)
NR	761 (36.3)	2 (68.0)	10 (31.4)	51 (38.0)	120 (32.7)	322 (37.9)	256 (35.9)
RNT	552 (24.6)	0 (0.0)	12 (31.9)	30 (20.3)	106 (27.2)	218 (23.9)	186 (24.6)
RTNG	404 (18.1)	0 (0.0)	5 (12.2)	17 (11.8)	78 (19.9)	155 (17.1)	149 (20.1)
DM II	919 (100.0)	0 (0.0)	16 (1.8)	43 (4.8)	142 (15.6)	385 (41.6)	333 (36.2)
NR	347 (38.1)	0 (0.0)	8 (52.5)	15 (35.9)	55 (39.7)	143 (37.3)	126 (37.8)
RNT	242 (26.3)	0 (0.0)	6 (36.1)	10 (21.6)	38 (26.5)	104 (27.5)	84 (25.1)
RTNG	192 (21.0)	0 (0.0)	1 (5.7)	7 (17.2)	31 (21.6)	79 (20.1)	74 (22.9)

NR, not recognized dyslipidemia; RNT, recognized dyslipidemia and not treated with lipid-lowering drugs; RTNG, recognized dyslipidemia and treated with lipid-lowering drugs and not at goal.

Table 6a

Unmet needs: prevalence of dyslipidemia without diagnosis or with inadequate (not at goal) or no lipid-lowering treatment

	Total N (%)	20–29 years N (%)	30–39 years N (%)	40–49 years N (%)	50–59 years N (%)	60–69 years N (%)	70–79 years N (%)
Total	4086 (100.0)	22 (0.6)	183 (4.8)	523 (13.6)	828 (20.6)	1447 (34.7)	1083 (25.8)
Unmet needs	3218 (80.3)	18 (84.6)	134 (76.4)	394 (78.2)	660 (81.4)	1140 (79.9)	872 (81.6)
NCEP risk class I	823 (100.0)	9 (1.3)	77 (9.3)	189 (23.6)	190 (23.5)	235 (28.0)	123 (14.4)
Unmet needs	445 (58.1)	7 (82.4)	37 (52.6)	109 (62.5)	116 (64.8)	124 (55.9)	52 (45.4)
NCEP risk class II	1040 (100.0)	9 (1.0)	58 (6.0)	164 (16.4)	269 (25.6)	390 (36.8)	150 (14.1)
Unmet needs	857 (84.5)	7 (81.2)	51 (90.2)	141 (88.0)	220 (83.8)	323 (84.6)	115 (79.0)
NCEP risk class III	2223 (100.0)	4 (0.2)	48 (2.3)	170 (8.1)	369 (16.8)	822 (36.2)	810 (36.4)
Unmet needs	1916 (86.9)	4 (100.0)	46 (96.3)	144 (86.0)	324 (88.6)	693 (84.8)	705 (87.8)

Table 6b

Unmet needs: prevalence of dyslipidemia without diagnosis

	Total N (%)	20–29 years N (%)	30–39 years N (%)	40–49 years N (%)	50–59 years N (%)	60–69 years N (%)	70–79 years N (%)
Total	4086 (100.0)	22 (0.6)	183 (4.8)	523 (13.6)	828 (20.6)	1447 (34.7)	1083 (25.8)
Unmet needs	1699 (45.6)	16 (77.2)	87 (53.9)	258 (55.3)	342 (45.9)	578 (43.2)	418 (41.2)
NCEP risk class I	823 (100.0)	9 (1.3)	77 (9.3)	189 (23.6)	190 (23.5)	235 (28.0)	123 (14.4)
Unmet needs	270 (38.5)	5 (64.7)	24 (37.2)	72 (45.3)	69 (42.0)	68 (33.4)	32 (29.7)
NCEP risk class II	1040 (100.0)	9 (1.0)	58 (6.0)	164 (16.4)	269 (25.6)	390 (36.8)	150 (14.1)
Unmet needs	536 (57.0)	7 (81.2)	37 (70.3)	105 (69.2)	127 (52.6)	196 (55.3)	64 (47.8)
NCEP risk class III	2223 (100.0)	4 (0.2)	48 (2.3)	170 (8.1)	369 (16.8)	822 (36.2)	810 (36.4)
Unmet needs	893 (42.6)	4 (100.0)	26 (58.7)	81 (52.4)	146 (42.8)	314 (39.9)	322 (41.7)

3.7. Unmet needs

Dyslipidemia without diagnosis from the treating physician or with inadequate or no lipid-lowering medical treatment ('unmet needs') were present in 80.3% of all patients with NCEP dyslipidemia, with no major differences across the age clusters. The majority of unmet needs result from patients with unrecognized disease (45.6% of the NCEP dyslipidemia patients) (Tables 6a and 6b).

3.8. Drug treatment

In the group of patients with treated dyslipidemia, the most frequently used lipid-lowering (LL) drug classes were statins (87%), followed by fibrates (10.2%), ezetimibe (4.4%), omega-3-FAs (4.1%), nicotinic acid derivatives (1.6%) and bile acid sequestrants (0.4%). The rates for fibrates were lower in NCEP risk class I (6.1%) than in classes II and III (12.6% and 10.5%, respectively). The rates for the use of statins were higher in the NCEP risk class III (88.9%) than in I and II (83.8% and 81.9%, respectively) (Fig. 3).

A total of 92.9% of the patients treated with lipid-lowering drugs received one, two (6.5%) or three (0.5%) different lipid-lowering compounds. Double combinations were mostly statin–ezetimibe combinations (3.1%) and statin–fibrate combinations (1.5%). Triple combinations were very rare and mostly statin–ezetimibe–omega-3-FA combinations (0.2%) (Table 7). Exactly 14.1% of all recognized patients received only lipid-lowering drugs; 50% received no lipid-lowering

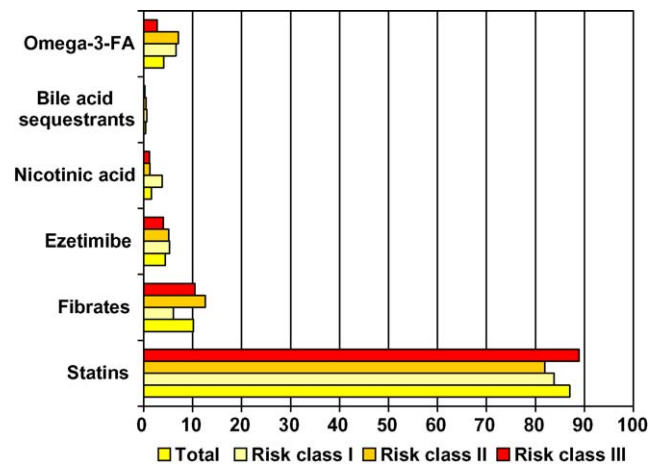


Fig. 3. Type of lipid-lowering medication across NCEP risk classes (as a % of patients with medical treatment).

drugs but did receive lifestyle interventions; 35.9% were treated with both approaches. The combined approach was used significantly more frequently in NCEP risk class III compared to classes I and II (Fig. 4).

4. Discussion

The present study had four key findings. First, in a group of unselected patients attending a primary care practice, approximately 50% could be classified as having a NCEP

Table 7
Combinations of lipid-lowering drug therapy

	N (%)
Two-drug combination	
Ezetimibe + omega-3-FA	2 (0.2)
Nicotinic acid + omega-3-FA	2 (0.2)
Statins + omega-3-FA	13 (1.2)
Statins + ezetimibe	36 (3.1)
Statins + nicotinic acid	3 (0.3)
Fibrates + nicotinic acid	2 (0.2)
Fibrates + statins	19 (1.5)
Three-drug combination	
Statins + ezetimibe + omega-3-FA	2 (0.2)
Statins + nicotinic acid + omega-3-FA	1 (0.1)
Statins + bile acid sequestrants + ezetimibe	1 (0.1)
Fibrates + statins + omega-3-FA	1 (0.1)
Fibrates + statins + ezetimibe	1 (0.1)

dyslipidemia. More than half of these patients were classified as being in the NCEP risk class III, and more than 60% were aged 60 years or older, with a continuous increase of dyslipidemia with age. Second, the prevalence of dyslipidemia merely based on physician diagnosis should be considered with caution. Only half of the NCEP-classified dyslipidemic patients in our sample were diagnosed as ‘dyslipidemic’ by their physicians. Third, the treatment and goal achievement rates for dyslipidemia were low. Only around 40% of recognized patients and only a quarter of all NCEP dyslipidemic patients were treated with lipid-lowering medications, with a significantly higher treatment rate in men compared to women. And fourth, only around 40% of the patients treated with lipid-lowering drugs achieved their NCEP treatment goals for LDL-C (10% of all dyslipidemic patients). In general, dyslipidemia in the elderly is more frequently diagnosed, but it is less frequently medically treated and at goal in this group. Compared to the overall group, the recognition and treatment rates in patients with CV diseases and diabetes were better, although goal attainment was worse. Interestingly, a remarkable number of the recognized dyslipidemic patients (14%) were treated solely with LL compounds without additional lifestyle intervention, which should be the basic therapy for these patients. The treating physicians however did not provide reasons for this decision and the corresponding patient data did not contain any other measure of lifestyle intervention indicating that this has been done by

intention (missing knowledge or ignorance of guidelines or simply patients non-compliance).

Unmet needs (no recognition of dyslipidemia, no or insufficient medical treatment) have been identified for approximately 80% of the dyslipidemic patients, with under-recognition as the major cause (approximately 45%).

These figures are alarming. If these point prevalence results are extrapolated to the entire patient population attending the over 60,000 primary care settings in Germany on an average day, around 1.8 million patients with dyslipidemia are seen by primary care physicians, but only 500,000 are treated with lipid-lowering drugs and only around 50,000 are at goal.

When these data from the primary care sector are compared to findings from population based cohort studies such as MONICA [11], PROCAM [10], or GRIPS [22], obviously more patients are suffering from dyslipidemia, even if different definitions for dyslipidemia have been used, such as the TC/HDL-C ratio in the MONICA cohort from 1984 to 1992. Our data however, in contrast to these investigations are representative for the entire primary care sector, and thus more relevant and applicable to daily life situations in clinical practice.

Moreover, the dyslipidemia prevalence assumptions used in our evaluation could even be worse. If we used the lower LDL-C goals of <70 mg/dl for patients at very high cardiovascular risk recommended by the British Hypertension Society (BHS guidelines) in the UK or published as a therapeutic option from the Coordinating Committee of the National Cholesterol Education Program (NCEP ATP III) in the USA, the numbers would be even higher [4,5]. There is an unequivocal agreement about the LDL-C goal of below 100 mg/dl for patients with CAD in the major guidelines [2,3,23]. They differ regarding recommendations for the prevention of cardiovascular events in asymptomatic high risk patients, notably in the strategy to be used for the risk assessment. For patients with lower NCEP risk classifications, for example, the European guidelines recommend an optimal LDL-C level of below 115 mg/dl, which would increase the estimate of dyslipidemic patients tremendously [2].

On the other hand, an overprediction of the Framingham risk function of approximately 50% could be shown in an evaluation of the German MONICA and PROCAM cohorts, which would mean a lower effective cardiovascular risk with

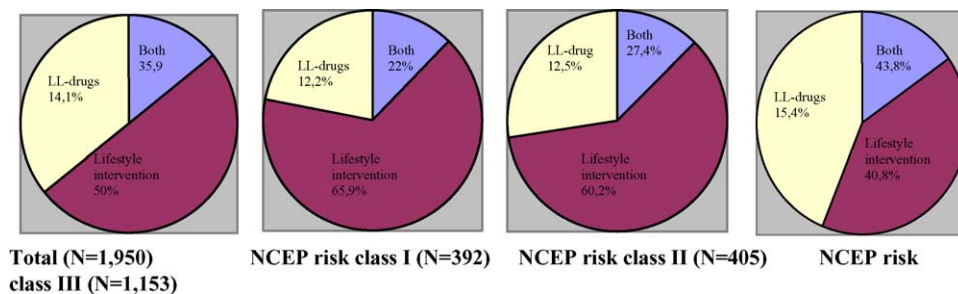


Fig. 4. Type of lipid-lowering therapy: lipid-lowering (LL) medication, lifestyle intervention, or both for diagnosed dyslipidemias.

accordingly higher LDL-C goals and thus lower prevalence rates for dyslipidemia in these patients. These results suggest the PROCAM risk calculator may be more appropriate for a German population [19]. Thus we felt it appropriate to calculate patient risk with the PROCAM risk calculator as well [19,21]. Using the PROCAM calculator for our population, we found slightly higher prevalence rates of dyslipidemia (57% PROCAM versus 54.3% Framingham), an identical physician diagnosis rate (54.4%), and similar treatment and goal achievement rates for dyslipidemia. 'Unmet needs' could be found in even more patients (82.3%) compared to the Framingham-based assessment (80.3%). Thus our data did not reveal any meaningful difference between the PROCAM and the Framingham risk calculations, clearly in disagreement with the findings by Hense et al. [19].

In our study, we used the Framingham-based NCEP guidelines for the definition and classification of dyslipidemia. The variety of national and international guidelines and definitions for those risk factors, however, requires additional comparative evaluations of data sets, especially in the primary care sector, to see which of the different guidelines and definitions best reflects the situation in Germany [23].

Of course the recommendation for lipid-lowering therapy as a minimum requirement for each patient with dyslipidemia would have tremendous cost implications, and health care systems have to carefully consider feasible ways to translate treatment recommendations into practical and cost-effective guidelines. This highlights the urgent need to further identify populations at risk which benefit in particular of lipid-lowering treatments, as the ASCOT study just recently did.

In ASCOT, a population at risk ($N=10,305$) defined as patients with hypertension and additional risk factors (e.g. mean LDL-C level 130 mg/dl), underwent lipid-lowering treatment with 10 mg of the HMG-CoA inhibitor atorvastatin and achieved a highly significant 36% reduction in combined cardiovascular risk (absolute risk reduction 1.1%, NNT 91) [24]. More realistic outcome trials with populations similar to the real-life primary care population such as used in ASCOT and performed in Germany are the next logical steps in translating the results from drug studies in highly controlled settings into daily clinical practice.

In summary, our results indicate that a significant proportion of patients in primary care are dyslipidemic and thus at increased risk for cardiovascular events. However, lipid-lowering therapy in this group of patients seems to be sub-optimal, clearly indicating the need of concerted efforts to improve treatment rates for elevated blood lipids.

Given the high prevalence of dyslipidemia in primary care, low recognition rates, low medical treatment and goal achievement rates, much could be achieved if recognition and subsequent treatment rates would increase and goal attainment, especially in secondary prevention, would improve. Plenty of room remains for improvement in prevention and treatment of cardiovascular disease in the primary care sector, as a pivotal part in the health care system.

Acknowledgments

Diabetes cardiovascular risk-evaluation: targets and essential data for commitment of treatment (DETECT) is a cross-sectional and prospective-longitudinal, nationwide clinical epidemiological study. DETECT is supported by an unrestricted educational grant of Pfizer GmbH, Karlsruhe, Germany. Principal investigator: Prof. Dr. H.-U. Wittchen; Staff members: Dr. H. Glaesmer, E. Katze, Dipl.-Math. J. Klotsche, Dipl.-Psych. L. Pieper, Dipl.-Psych. A. Bayer, Dipl.-Psych. A. Neumann. Steering Committee: Prof. Dr. H. Lehnert (Magdeburg, London), Prof. Dr. G.K. Stalla (München), Prof. Dr. M.A. Zeiher (Frankfurt); Advisory Board: Prof. Dr. W. März (Graz), Prof. Dr. S. Silber (München), Prof. Dr. U. Koch (Hamburg), PD Dr. D. Pittrow (München/Dresden).

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