Physicians’ perception of guideline-recommended low-density lipoprotein target values: characteristics of misclassified patients

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Aims
The present study investigated the awareness of primary care physicians for patient characteristics relevant for designation of low-density lipoprotein (LDL) target values.

Methods and results
Physicians (n = 907) were asked to estimate guideline-recommended LDL target value for 30 of their patients with hyperlipidaemia. In total, 25,250 patients were allocated on that basis in three different groups (LDL target <100, <130, and <160 mg/dL), in which by guideline criteria 68.0, 21.9, and 10.1% of patients, respectively, were allocated. We analysed (by logistic regression) whether physicians utilized risk factors and co-morbidities appropriately for assignment of correct LDL target values. Overall, physicians estimated recommended LDL target values correctly in 55.1% of male vs. 49.1% of female patients (P < 0.001). In the group with LDL targets of <100 mg/dL, correct assignment was most often given to male patients with a history of myocardial infarction (MI; 77.1%). In comparison with this group, increasing probabilities for incorrect assignment were found in patients with documented coronary artery disease (CAD) without a history of MI [odds ratio (OR): 2.08, 95% confidence intervals (95% CI): 1.87–2.33], CAD-equivalent conditions (OR: 2.30, 95% CI: 2.08–2.55), and a 10-year risk based on calculated risk scores (OR: 2.69, 95% CI: 2.40–3.02). Next, physicians were grouped, based on the number of correct assignments they gave to their patients, in quartiles of guideline knowledge. In patients from physicians of the top performing quartile (90% of correct assignments), LDL levels were significantly lower than in the second, third, and fourth quartiles (LDL 134.3, 138.8, 145.5, 151.4 mg/dL, P < 0.001 between all groups).

Conclusion
In primary care, about half of high-risk patients receive correct assignment of guideline-recommended LDL targets by their physicians. Perception of correct LDL target values varied largely depending on patients’ gender and co-morbid conditions. Poor perception of risk resulted in lower rates of objective LDL target achievement.

Keywords
Cardiovascular risk • Hyperlipidaemia • Lipid-lowering treatment • Primary prevention • Secondary prevention

Introduction
Hyperlipidaemia is a major risk factor for the development of atherosclerosis.1–3 Cholesterol lowering by means of lifestyle changes and pharmacotherapy results in a marked reduction of cardiovascular events.4–13 In pharmacological studies, pre-defined low-density lipoprotein (LDL) target values were reached in up to 83% of patients.14,15 In view of these excellent treatment options, the management of hyperlipidaemia takes a pivotal role in national and international guidelines and recommendations for primary and secondary prevention of cardiovascular disease.16–19 The intensity of cholesterol-lowering treatment depends not only on the LDL cholesterol level in a given patient, but also on the estimated overall cardiovascular risk of this individual.
The higher the risk of a cardiovascular event, the lower LDL target values are supposed to be according to guidelines. However, these target values are not adequately attained in everyday clinical routine. The reasons for this dilemma are complex and had been subject of several studies. The physicians’ knowledge of the guideline-recommended LDL target values and definition of the appropriate treatment goals may be of major importance in this process. Particularly, when physicians estimate LDL targets incorrectly, this error may frequently result in insufficient treatment and thus LDL values are higher than those recommended by guidelines. Therefore, misperception of conditions defining LDL goals may lead to an elevation of overall cardiovascular risk of respective patients. The current study is intended to elucidate the extent to which risk factors, morbidities, and other patient-specific characteristics escape the physicians’ attention, resulting in inappropriate assignment of LDL target values.

**Methods**

**Patient sample**

The Manage Lipids Study is a survey on treatment standards in patients with hyperlipidaemia. Between October and December 2004, a total of 907 German primary care physicians were asked to provide data on 30 of their patients with hyperlipidaemia requiring treatment (diet and/or medication). The selection of patients and their treatment was left to the discretion of the managing physician. All participating practitioners used their knowledge of the patient to estimate the cardiovascualr risk subjectively. It was also left to the discretion of the physicians to use a risk assessment chart or scoring table.

Physicians used the same laboratories as in their usual clinical routine. Lipid profiles of 25 250 patients were documented centrally. In detail, the 12 h fasting values for total cholesterol, LDL, high-density lipoprotein (HDL), and triglycerides were measured. Moreover, demographic data such as age, gender, height, weight, and body mass index (BMI) were recorded on standardized documentation forms by the physicians. Information on the following patient parameters was documented systematically with respect to (i) clinical history (history of: myocardial infarction (MI), coronary artery disease (CAD), coronary artery bypass grafting (CABG), peripheral artery disease (PAD), stroke, or transient ischaemic attacks (TIA)) and (ii) a history of major cardiovascular risk factors (smoking habits and positive family history in respect of CAD, defined as the primary manifestation of CAD in first-degree male relatives before the 55th first-degree female relatives before the 65th year of life), (iii) physical examination (blood pressure with or without antihypertensive medication) and (iv) laboratory tests (diabetes mellitus: blood glucose and HbA1c; diabetic nephropathy defined as at least microalbuminuria). In essence, the assessment of an individual patient’s risk as estimated by the physician and the objective criteria were based on the same information. The information from the patients’ clinical history relevant for our analyses was the diagnosis that was documented in the charts of the physician. Thus, no further measures were taken to verify this information. The study protocol was approved by the Ethics Commission of the University of Lübeck.

**Low-density lipoprotein target values**

All physicians had access to the same data that were utilized by the study centre for calculation of the National Cholesterol Education Program—Adult Treatment Panel III (NCEP ATP-III) LDL target value. This guideline provides similar recommendations as the ones of the German Cardiac Society. In brief, guideline-recommended LDL target values are <100 mg/dL for patients with (i) CAD, (ii) a CAD equivalent, or (iii) a 10-year risk for a cardiovascular event of >20%. Non-coronary vascular diseases such as PAD, stroke or TIA, and diabetes mellitus are regarded as CAD equivalent. In accordance with the NCEP-III guideline, the 10-year risk of developing CAD was calculated with the Framingham risk score. Low-density lipoprotein target values <130 mg/dL applied to patients with two or more vascular risk factors. The NCEP ATP-III guideline specifies smoking, arterial hypertension (defined as blood pressure >140/90 mmHg or intake of antihypertensive medication), an HDL cholesterol <40 mg/dL (if the HDL cholesterol is >60 mg/dL, the number of cardiovascular risk factors is reduced by 1), a positive family history for CAD, and age (≥45 years in men and ≥55 years in women) as risk factors. Moreover, this LDL target value applies to patients with a 10-year risk of developing CAD between 10 and 20% as estimated by the Framingham risk score. Low-density lipoprotein target values <160 mg/dL apply to patients with no or with only one vascular risk factor and a 10-year risk of CAD <10% according to the Framingham risk score.

**Statistical analyses**

All statistical analyses were performed by using SAS software (version 8.2). Continuous variables were compared by Kruskal–Wallis tests for comparison of independent samples and post hoc analyses using Fisher’s least significant difference test. Categorical variables were compared between groups using the χ² test. In the group with an LDL target value <100 mg/dL, the χ² test was added to the χ² analysis. In the group with an LDL target value <160 mg/dL according to the guideline, a logistic regression model was developed with LDL target assignment by the physician (correct vs. incorrect) as dependent variable and age, gender, BMI, hypertension, a positive family history of CAD, smoking status, diabetes, diabetic nephropathy, CAD, MI, CABG, TIA, and PAD as explanatory variables. Odds ratios, 95% CI, and two-tailed P-values of the Wald χ² test are presented. Statistical significance was accepted at P-values <0.05.

**Results**

**Patient characteristics**

By NCEP ATP-III guideline criteria, LDL targets of <100, <130, and <160 mg/dL were applicable to 68.0% (n = 17 227), 21.9% (n = 5551), and 10.1% (n = 2472) of patients with hyperlipidaemia, respectively. The demographic data of these patients are shown in Table 1. In accordance with the stratification criteria for an LDL target value <100 mg/dL, all patients with a CAD or a CAD-equivalent condition were in this group. Patients with an LDL target value <100 mg/dL were older when compared with those with an LDL target value <130 or <160 mg/dL, were more often male, had a higher BMI, and were more frequently hypertensive.

**Low-density lipoprotein values estimated by the managing physicians**

In the overall patient sample of the Manage Lipids Study (n = 25 250), physicians estimated guideline-recommended LDL target values correctly in 52.4% of their patients. The correct assignment of guideline-recommended LDL targets was given to 55.1% of male and 49.1% of female patients, respectively (P < 0.001).
The highest percentage of patients with correctly estimated LDL target values was found in the group with an LDL target value of less than 100 mg/dL (n = 17,227, 57.4% correct estimates; Figure 1A). The LDL target values of less than 130 mg/dL (n = 5,551, 41.7% correct estimates; Figure 1B) and less than 160 mg/dL (n = 2,472, 41.7% correct estimates; Figure 1C) were significantly less often assigned correctly by physicians in accordance with the guideline (P < 0.001 for each vs. the group with an LDL target value < 100 mg/dL).

In about 40% of the patients with an LDL target value < 100 mg/dL (Figure 1A) and < 130 mg/dL (Figure 1B), the estimation by the physicians was significantly less often correct compared to the group with an LDL target value < 100 mg/dL.

Table 1: Baseline demographics of hyperlipidaemic patients with low-density lipoprotein target values of <100, <130, and <160 mg/dL according to NCEP ATP-III guideline (mean ± SD; CAD, coronary artery disease; PAD, peripheral artery disease; TIA, transient ischaemic attack)

<table>
<thead>
<tr>
<th>LDL goal &lt;100 mg/dL (n = 17,227)</th>
<th>LDL goal &lt;130 mg/dL (n = 5,551)</th>
<th>LDL goal &lt;160 mg/dL (n = 2,472)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 65.6 ± 10.1</td>
<td>58.1 ± 12.0</td>
<td>60.3 ± 12.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gender (% male)</td>
<td>59.2</td>
<td>46.0</td>
<td>37.7</td>
</tr>
<tr>
<td>Body mass index 28.1 ± 4.3</td>
<td>26.8 ± 3.8</td>
<td>26.5 ± 3.7</td>
<td>0.001</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>83.4</td>
<td>68.0</td>
<td>54.0</td>
</tr>
<tr>
<td>Smoking (current, %)</td>
<td>23.4</td>
<td>28.2</td>
<td>11.3</td>
</tr>
<tr>
<td>Family history of CAD (%)</td>
<td>21.5</td>
<td>27.6</td>
<td>13.0</td>
</tr>
<tr>
<td>Coronary artery disease (%)</td>
<td>52.4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Myocardial infarction (%)</td>
<td>22.9</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Coronary bypass surgery (%)</td>
<td>14.2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>54.7</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Diabetic nephropathy (%)</td>
<td>7.4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Apoplex/TIA (%)</td>
<td>11.9</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>PAD (%)</td>
<td>13.0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Figure 1 (A–C) Low-density lipoprotein target values estimated by the managing physicians for patients with objective low-density lipoprotein target values <100 mg/dL (A), <130 mg/dL (B), and <160 mg/dL (C) as assigned by the NCEP ATP-III guideline criteria, respectively. Patients that were assigned correctly to their low-density lipoprotein target values are shown in black, grey symbols show too high and white too low low-density lipoprotein estimates by physicians.
managing physician was higher than the objective target value. By contrast, physicians estimated LDL target values lower than those recommended by the guidelines in about 20% of patients whose LDL target value was <130 mg/dL (Figure 1B). Interestingly, this number of falsely low-estimated LDL values increased to >50% in those with an LDL target value <160 mg/dL (Figure 1C).

**Characteristics of misclassified high-risk patients (low-density lipoprotein target value <100 mg/dL)**

The greatest consistency between the LDL target values estimated by the managing physicians with those assigned by guideline criteria was observed in patients with known CAD (Figure 2). The percentage of correctly estimated LDL target values was substantially lower if a CAD-equivalent condition was the guideline criterion for the LDL target value <100 mg/dL. A 10-year risk >20% for developing CAD based on the Framingham risk score without prevalent disease manifestation was practically not perceived for correct assignment of an LDL target value <100 mg/dL (P < 0.001 between three groups, Figure 2).

The highest rates of correct assignment of LDL targets of <100 mg/dL were found in patients with a history of MI, CAD, and diabetes mellitus as concomitant disease, and CAD with a history of CABG (Figure 3). Interestingly, in all patients' groups with CAD, the LDL target value was correctly estimated more often in men than in women (67.6 vs. 59.7%; P < 0.001; Figure 4). A similar gender difference was observed when a CAD-equivalent condition defined the LDL target value or when a 10-year risk >20% for developing CAD on the Framingham risk score defined the LDL target value (Figure 4). Likewise, female compared with male patients with a history of MI more frequently had incorrect assignment to low LDL targets in a multivariate model adjusted for hypertension, smoking status, and a family history for CAD (OR: 1.32, 95% CI: 1.12–1.55; P < 0.001, Figure 5).

**Clinical implications on incorrect estimations of low-density lipoprotein target values**

In order to evaluate the clinical implication of incorrect estimation of LDL target values, we determined the percentage of correctly assigned patients for each physician and grouped physicians in quartiles of guideline knowledge. The best quartile (Q1, n = 227) of physicians estimated the target values of their patients correctly in 90.1–100% of their patients, the second quartile (Q2, n = 227) in 66.8–90%, and the third (Q3, n = 227) in 40.8–66.7%. The worst quartile (Q4, n = 227) estimated target values correctly in <40.8% of their patients. The percentage of patients assigned to a given treatment target based on objective criteria and physicians estimates is shown in Table 2. Figure 6A displays the measured LDL levels in patients with objective target values of <100 mg/dL. The achieved LDL-cholesterol level in patients was highly correlated with the performance of physicians in estimating their patients'
The analysis shows data of patients with a recommended low-density lipoprotein target value <100 mg/dL by NCEP ATP-III guideline criteria. The proportion of men (black) and women (grey) with correctly (<100 mg/dL; upper half) and incorrectly estimated low-density lipoprotein values (≥100 mg/dL; lower half) in patients with manifest coronary artery disease, a coronary artery disease equivalent [defined by the presence of peripheral artery disease (PAD), stroke, transient ischaemic attack (TIA), or diabetes mellitus] or a 10-year event risk >20% based on the Framingham risk score.

**Figure 4**

Odds ratio (square) and corresponding confidence intervals (lines) for incorrectly estimated low-density lipoprotein values in different subgroups of patients with recommended low-density lipoprotein target values of <100 mg/dL. Results are demonstrated in comparison with male patients with a history of myocardial infarction (MI). The results for male patients are marked in black; results for female patients are marked in grey. (CAD, coronary artery disease).
target values, e.g., those physicians who estimated target values in their patients more precisely presented patients with lower LDL levels. After a period of 3 months given to the physicians for treatment optimization, the same pattern was still seen in the four groups, although overall lower levels were found (Figure 6B).

Discussion

In every day practice, primary care physicians need to estimate a patient’s cardiovascular risk in order to assign the patient to the adequate treatment goal. Our study demonstrates that primary care physicians estimated recommended LDL target values correctly in only about half of their patients with hyperlipidaemia. Our report is in agreement with a similar survey of general practitioners’ subjectively grading their patients in Italy. Our study furthermore demonstrates that the assignment of correct target values markedly differs depending on co-morbidities and gender. Alarmingly, women with a documented history of MI or diabetes mellitus are less frequently assigned to the high-risk group than respective men. Finally, our data suggest that physicians who fail to assign correct target values to their patients provide less adequate treatment.

It was reported that major determinants of general practitioners’ underestimation of cardiovascular risk were age, gender, and smoking habits. There is also much evidence suggesting that physicians’ attitudes and beliefs about statins, hyperlipidaemia, and treatment goals may influence how guidelines are translated into clinical practice. Our study highlights other causes for suboptimal treatment as it identifies patient characteristics that carry the highest probability of being overlooked for adequate lipid-lowering treatment. Recommended target values were more often sufficiently estimated in patients with known CAD, in particular, when the history included MI or coronary bypass surgery. In contrast, correct estimation was less frequently reported in patients with CAD-equivalent conditions (such as PAD, stroke, TIA, or diabetes mellitus) or a high risk (>20%) of developing CAD based on risk calculation using the Framingham risk score.

In high-risk patients, i.e., the patients’ group with LDL target values <100 mg/dL, the guideline-recommended treatment goals were less often sufficiently estimated in women (across all subgroups studied). Gender disparities in CAD outcomes in women have been documented before, but the reasons remain unclear. Here, we provide data strongly supporting the notion that inadequate perception of a woman’s risk across a wide spectrum of co-morbidities might contribute to this gender difference. Furthermore, our findings are in line with other investigations according to which women with symptomatic CAD are more often overlooked for risk stratification. Taken together, the data suggest that often primary care physicians do not associate female gender with the potentially fatal cardiovascular complications even if MI or diabetes is known from the patients’ history.

A large subsample studied here displayed high-risk criteria (such as multiple risk factors) other than known CAD and thus had an indication for low LDL treatment targets. Interestingly, in less than one-fifth of respective patients’, the guideline-recommended LDL-target level was perceived correctly. A possible explanation might be that standardized and well-established risk scores such as the Framingham or PROCAM score are not utilized routinely by primary care physicians in Germany.

As expected, the highest number of patients with correctly specified LDL target levels was found in the group of CAD patients. Of note, co-morbidities such as MI, coronary artery
bypass surgery, as well as diabetes further increased the chance for correctly specifying LDL target values. These findings indicate that physicians are sensitive for aggressive treatment of such co-morbidities, implying a worse long-term outcome and a potentially strong benefit by treatment of hyperlipidaemia.

In the present study, physicians who misperceived a high-risk profile in their patients more frequently presented with worse LDL-cholesterol profiles in their patients. We specifically analysed the group of patients with low LDL treatment targets and observed that LDL levels in such patients of physicians with good or poor guideline knowledge differed by $>17 \text{mg/dL}$ on average. Thus, the failure of a physician to acknowledge a patient’s risk correctly may contribute to less adequate treatment. Our investigation is in line with several studies which evaluated the treatment pattern and the attainment of lipid targets with respect to the current recommendation of the National Cholesterol Education Panel and clearly documents shortcomings in the guideline implementation.

Little is known on the mechanisms accounting for such insufficient risk stratification. One explanation is that laboratories provide ‘normal ranges’ for LDL cholesterol, which, however, do not always match with the latest guidelines and certainly do not respect all individual risk factors. This information might cause confusion among both physicians and patients. One might also speculate that the rapid modifications of treatment guidelines and their broad-scale implications for primary care physicians dealing with ambulatory patients constitute an enormous challenge. Indeed, the introduction of new medications and an increasing knowledge obtained from large-scale therapy studies confront physicians with constantly modified treatment goals in frequently revised versions of the guidelines. Fortunately, the latest Euro Heart survey indeed demonstrates improving numbers for utilization of statins and achievement of target values in patients with CAD.

**Study limitations**

The design of the study carries a number of limitations. The choice of patients to be included in the study was left to the managing physicians. In theoretical terms, this entails the possibility of a selection bias. Moreover, the participating physicians had the chance to read the guidelines and to assign LDL target values in their patients accordingly. Such behaviour might have increased the number of correct assignments in this study but not reflect the routine management of patients. Given this potential bias, knowledge of the guidelines may be less good than that reported in our investigation. On the other hand, the use of guidelines or risk calculators is being recommended so that the conditions used in our study may reflect the best case scenario. Furthermore, the contact with physicians was via employees of a pharmaceutical company. Consequently, physicians may have had a strong motivation to provide intensive recognition to guideline adherence. This possible limitation also tends to overestimate the quality of guideline implementation. On the other hand, the design chosen allowed generating an enormously large data set. In this respect, the marked differences observed between genders and defining risk conditions with respect to LDL target assignment should not be affected by such potential bias.

**Conclusion**

The present study shows sizable deficits in physicians’ perception of patient characteristics that define recommended LDL target values, particularly, but not exclusively, in women. Moreover, lower appreciation of guideline targets by physicians is related to higher LDL cholesterol values in their patients. Thus, efforts should be made to increase the applicability of guidelines. In particular, instruments identifying high-risk patients more easily should be developed. Special attention should be paid to women and patients without known cardiovascular disease but with accumulation of vascular risk factors or CAD-equivalent conditions, since both groups frequently escape their physicians’ perception for aggressive lipid-lowering therapy.

**Conflict of interest**: none declared.

**References**


Physicians’ perception of guideline-recommended LDL target values


