INCREASED ATHEROSCLEROTIC PLAQUE BURDEN IN ANGIOGRAPHICALLY NEAR-NORMAL CORONARY SEGMENTS IN PRIMARY HYPERLIPIDEMIC PATIENTS WITH SIGNIFICANT CORONARY ARTERY DISEASE

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Objective: The aim of this study is to evaluate atherosclerotic plaque burden in angiographically near-normal coronary segments and to identify the factors associated with the progression of atherosclerotic plaque in primary hyperlipidemic patients. Methods: 19 patients with primary hyperlipidemia (12 FH patients and 7 non-FH patients) were studied. Angiographically near-normal 19 proximal coronary segments from each patients (mean length 18.2 ± 2.2mm) were evaluated by ECG gated three-dimensional intravascular ultrasoud (3D-IVUS). Quantitative measurements of vessel volume (VV) and lumen volume (LV) (mm^3) were performed semi-automatically, and plaque volume (PV=VV-LV) and PV/LV ratio were calculated. Each value was compared between two groups with and without significant CAD defined as showing ≥75% stenosis in at least one segment on coronary angiography. Results: In the CAD group, LV was significantly smaller (CAD 168 ±82 vs non-CAD 241±70 mm^3, p=0.046) and PV/LV ratio was significantly greater (CAD 0.74±0.28 vs non-CAD 0.49±0.14, p=0.039) than non-CAD group, while no significant differences were observed in VV and PV between two groups. There was stronger correlation between LV and PV (r=0.846, p=0.016) in the CAD group, reflecting positive remodeling, than in the non-CAD group. Among conventional risk factors, only HDL-cholesterol level showed tendency of negative correlation with PV/LV ratio (r=-0.434, p=0.056) Conclusion: These results suggest that atherosclerotic plaque burden is potentially greater in patients with significant CAD than in those without CAD.

THYROID FUNCTION AND ANGIOGRAPHICALLY ASSESSED CORONARY ATHEROSCLEROSIS

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Background: Ssubclinical hypothyroidism is a strong indicator of risk for aortic atherosclerosis and myocardial infarction. We hypothesized that variation of thyroid function within the normal range may influence the presence and severitiy of coronary atherosclerosis.

Methods: We studied a total of 100 consecutive men and women (59 men, 41 women, age 63.7+/-11.0 years) who underwent coronary angiography. Blood from these patients was tested for serum thyrotropin concentrations, and for free tri-iodothyronine and free thyroxine concentrations. In addition to the assessment of thyroid function, angiographic results of coronary artery assessment were obtained. CAD severity was scored as 0 for those with smooth normal epicardial coronary arteries, 0.5 for plaquing (<50% diameter stenosis), and 1, 2, or 3 for those with single-, double-, or triple-vessel epicardial coronary artery stenosis of >50%, respectively.

Results: Higher levels of serum free thyroid hormone concentrations were associated with decreased severity of coronary atherosclerosis. Serum free tri-iodothyronine was 2.99 +/- 0.33 pg/mL in patients with a CAD severity score of 0 to 1 and 2.74 +/- 0.49 pg/mL in patients with a CAD severity score of 2 and 3 ($P<0.01$). Moreover, serum free thyroxine concentrations showed a trend to higher levels in CAD severity score 0 to 1 patients compared to CAD severity score 2 and 3 patients. Higher levels of serum thyrotropin concentrations were associated with increased severity of coronary atherosclerosis (1.37 +/- 1.02 mU/L versus 1.98 +/- 2.13 mU/L in severity score 0 to 1 versus CAD severity score 2 and 3 patients; p=0.049).

Conclusion: These data in patients referred for coronary angiography suggest that variation of thyroid function within the statistical normal range may influence the presence and severity of coronary atherosclerosis.

THE GAP BETWEEN TREATMENT GUIDELINES AND ROUTINE CARE TREATMENT PATTERNS IN THE MANAGEMENT OF HIGH RISK PATIENTS: FINDINGS FROM THE DETECT STUDY

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Several approaches to the primary and secondary prevention of cardiovascular diseases have successfully been evaluated clinical trials. Yet, according to recent large-scale studies, only a fraction of the patients needing treatment in primary care seem to be recognized and receive adequate treatment. The epidemiological study DETECT (*D*iabetes Cardiovascular Risk *E*valuation: *T*argets and *E*ssential Data for *C*ommitment of *T*reatment) was launched to identify the reasons, the extent and the short-term consequences of unmet needs in patients with high cardiovascular risk.

DETECT is a large multistage cross-sectional and prospective 12-month study of 70000 consecutive patients in over 3000 primary care offices, nationwide. Here, we report on the findings from a subset of approximately 7500 patients characterized by an extensive standardized laboratory program with focus on the risk assessments and treatment modalities of lipid disorders in patients with coronary heart disease (CHD) and/or type 2 diabetes mellitus (DM).

According to the NCEP ATPIII guidelines the majority of the patients (52.6 %) was in the category with a high risk for CHD. More than 78 % of these patients did not achieve the goal for LDL cholesterol (< 100 mg/dL). The proportion of patients reaching LDL-C targets is lowest in patients at highest risk of CHD and highest in patients at low risk. Only half of the patients with CHD, one third of the patients with type 2 diabetes and only one quarter of patients with a global ten-years risk > 20 % receive lipid lowering drugs. The physicians´ awareness of the patients´ individual target value is closer to NCEP targets than actual LDL-C concentrations. Under-treatment therefore may not be due to lacking physicians´ awareness of therapeutic needs, but due to pressure built up by healthcare authorities.

RISK CATEGORISATION OF PATIENTS WITH HYPERCHOLESTEROLAEMIA: NATIONAL CHOLESTEROL EDUCATION PROGRAM ADULT TREATMENT PANEL III VERSUS II.

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Introduction: The Third Report of the Expert Panel on Detection, Evaluation and Treatment of hypercholesterolaemia in adults (Adult Treatment Panel [ATP] III) differs in several ways from ATP II guidelines. Several advances in ATP III focus on concept of risk which moves away from the old concept of primary and secondary prevention and the designation of other high risk groups for secondary prevention known as CAD risk equivalents.

Objective: To compare the risk categorisation according to NCEP ATP III and ATP II guidelines in patients with Familial Hypercholesterolaemia (FH). **Design and Methods**: A total of 135 FH patients (80 females, 55 males, mean ± SD age: 44.8 ± 12.6 years) were recruited in this cross sectional study. Diagnosis of FH was made based on Simon Broome's criteria. 121/135 patients (89.6%) had definite FH and 14/135 patients (10.4%) had possible FH. The risk assessment were conducted in these patients and they were categorised into 3 groups: low, moderate and high risk according to NCEP ATP III and ATP II guidelines. **Results**: In all FH patients, 84/135 (62.2%), 33/135 (24.4%) and 18/135 (13.3%) were categorised as low, moderate and high risk respectively by ATP III compared to 2/135 (1.5%), 2/135 (1.5%) and 131/135 (97.0%) by ATP II. Among the definite FH patients, 76/121(62.8%), 29/121 (24.0%) and 16/121 (13.2%) were categorised as low, moderate and high risk respectively by ATP III compared to 3/121(2.5%), 1/121 (0.8%) and 117/121 (96.7%) by ATP II. Among the possible FH patients, 8/14 (57.1%), 4/14(28.6%) and 2/14 (14.3%) were categorised as low, moderate and high risk respectively by ATP III compared to 2/14 (14.3%), 2/14(14.3%) and 10/14 (71.4%) by ATP II. **Conclusion**: ATP III and ATP II guidelines differ greatly in the proportion of FH patients categorisation as high risk category. As FH patients are at higher risk of developing premature coronary heart disease, the categorisation of definite FH patients as high risk category possibly need to be readdress.

ATTAINMENT OF PHYSICIAN SET TARGET TOTAL CHOLESTEROL GOALS IN SWITZERLAND AMONG PATIENTS TREATED WITH LIPID LOWERING DRUGS

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Objective: Cholesterol reduction to levels below currently recommended goals have shown to reduce CHD events. This study aimed to assess total cholesterol (TC) goal (defined by treating physician for each patient) attainment among CHD and CHD equivalent patients prescribed lipid-lowering drugs (LLD) in Switzerland. **Methods:** This was a multicenter retrospective observational study, 99 centers (77% primary care centers and 23% specialist centers) across Switzerland were recruited at random to participate in the study. Each center recruited all patients seen during a five consecutive day period. Medical records were reviewed by physicians to collect data about patient characteristics, baseline and follow-up laboratory values, treatment, and resource use. **Results:** A total of 1218 patients prescribed LLD were included in the current analysis. 49.6 % were CHD patients, 22.9%were CHD equivalent patients, 27.5 % were non-CHD patients with 2 + major risk factors and 11.8% were non-CHD patients with < 2 major risk factors. The mean (SD) baseline age for the 4 patient groups listed above were; 68.7(10.2), 64.3(11.8), 59.9(11.4), 60.01 (14.6), mean (SD) baseline TC in mmol/l for each group were; 7.02 (1.2), 7.04 (1.1), 6.7 (1.1), 7.16 (1.5) and the mean physician set TC goals in mmol/l for each group were; 4.9 (0.5), 5.00 (0.5), 5.1 (0.6) 5.16 (0.54). The TC goal attainment rate of CHD and CHD equivalent patients was approximately 35% and 33%. **Conclusion:** Majority of CHD and CHD equivalent patients treated for cholesterol lowering in Switzerland do not attain physician set target lipid levels with current LLD. More effective lipid lowering treatment is required in these patients.

THE ROLE OF PHYSICIAN'S PREFERRED LIPID TARGETS IN THE MANAGEMENT OF PRIMARY HYPERCHOLESTEROLEMIA IN CANADA.

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Our objective is to investigate the impact of prescribing physicians' preferred LDL-C targets on their patients' goal attainment in Canada using data from a cross-sectional study in patients with hypercholesterolemia. Of 3,172 statin users initially not at recommended LDL-C goal, 29% were still not achieving targets at the time of the visit, a quarter of whom being perceived by their physician as having reached goal. Overall, targeted LDL-C levels differed than those recommended in 34% of patients, with one third treated to less aggressive and the remaining to more aggressive targets. Patients treated less aggressively were at increased risk of not reaching goal (RR=1.82; 95% CI=1.63-2.04). These results indicate that a significant discrepancy exists between perceived target LDL-C levels and those recommended in treatment guidelines.

SUB-OPTIMAL MANAGEMENT OF PRIMARY HYPERCHOLESTEROLEMIA IN CANADA

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The objective of this analysis is to characterize statin-treated patients not at LDL-C goal and to identify barriers in effective lipid management in Canada. CALIPSO is a cross-sectional study to ascertain current statin prescribing patterns of a selection of physicians and to determine effectiveness in reaching goal in patients with hypercholesterolemia. Of 3,172 statin users initially not at recommended LDL-C goal, 29% were still not achieving targets at the time of the visit. The vast majority of patients not at goal (95%) were at high risk of CHD and required a greater reduction in LDL-C at treatment initiation than those at goal (41% vs. 29% respectively; p<0.001). 27% were already using a high dose of statin at the time of the visit and for 78% of them, titration was judged not to be an option. There appears to be a need for an alternative to statin titration that provides better efficacy without compromising safety and tolerability.

TIME TO LDL-CHOLESTEROL GOAL ATTAINMENT IN SPAIN

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Background: Majority of patients treated for hyperlipidemia with currently available cholesterol lowering drugs (LLD) do not achieve recommended LDL-C goal in Spain. **Objective:** To assess LDL-C reduction and goal attainment over time and determine the time period when patients are most likely to attain goal after initiation of LLD in Spain. **Method:** Retrospective cohort study was conducted at 23 primary care and 16 outpatient lipid centres. Eligible patients were adults (>=18 years) with CHD/CHD equivalent or 2+ major risk factors (2+RF) prior to first prescription of LLD between 01/98 - 04/99, and +36 months of follow-up data. LDL-C goals were based on NCEP III guidelines (100 mg/dl for CHD/CHD equivalent patients, and 130 mg/dl for 2+RF group). Goal attainment analyses were based on the proportion of patients at goal from those with a valid LDL-C measure at three months time intervals from therapy start, and on the increase or decrease in that proportion for subsequent periods.**Results:** 619 patients (46% CHD/CHD equivalent and 54% nonCHD with 2+ RFs) were included. Mean age was 60 years (SD 10.22), 48% were female. Statins were initial LLD in 90% patients. Only 20% CHD and 29% 2+RF patients were at goal at study end. The proportion of patients at goal increased to 23% at 3 months from therapy start (fig.1), remaining stable afterwards. Increase in the proportion of patients at goal was only positive for this period (p<0.05) (fig.2).**Conclusions:** The percentage of patients at goal only increased during the first three months period from therapy start, remaining flat there after. More aggressive lipid lowering therapy should be started for those not at goal after first three months from LLD start, to enable more patients to get to LDL-C goal.

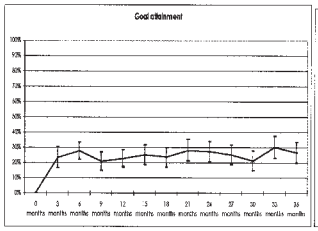

Figure 1

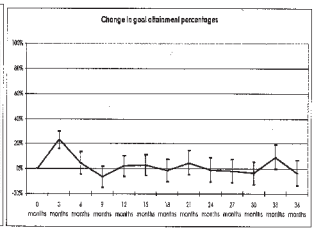

Figure 2

CHOLESTEROL GOAL ATTAINMENT IN DYSLIPIDEMIC TREATED PATIENTS AND INCIDENCE OF CARDIOVASCULAR EVENTS IN CLINICAL PRACTICE

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Objectives: To investigate in French primary care, the association between LDL-cholesterol goal (LDL-C <130 mg/dL based on therapeutic objectives (TO) stated in national guidelines) attainment and occurrence of cardiovascular (CV) events in multiple CV risk factor (3) patients, without coronary heart disease history. **Methods:** 579 patients treated with LLD for 3 years and with a yearly documented LDL-C (2000-2002) were consecutively included by 236 GPs. Based on number of years patients attained TO during 3 years follow-up they were grouped into: TO+++(all 3 year; n=145), TO intermediate (only part of the time; n= 256), and TO---(never; n=178). CV events (angina, MI, heart failure, stroke, peripheral arteritis) in the last year of follow-up (2002) were collected via computerized medical records (Thales database) and specific physician questionnaire. The risk of CV events was studied according to TO status. Logistic regression analysis was used to adjust for baseline differences in risk factors. **Results:** Only 25% patients reached TO during all three years. Patients with at least one CV event in 2002 were 5.5%, 10.5% and 12.9% respectively in the TO+++, TO intermediate and TO--- groups. Compared to TO+++ patients, significantly increased risks of CV event in 2002 were observed, both for TO intermediate (OR=2.34, 95% IC=[1.01-5.39]) and TO --- patients (OR= 2.99, 95% CI=[1.26-7.08]). **Conclusion:** This study confirms that inadequate LDL-C goal attainment in high CV risk patients treated with LLD is associated with an increased incidence of cardiovascular morbidity. Our results strongly support the necessity of a better adherence to guidelines to improve cardiovascular prevention.

PROJECTED BENEFIT OF EZETIMIBE IN CHD PATIENTS NOT AT LDL-C GOAL WITH CURRENT STATIN THERAPY IN GERMANY.

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Background: Even with statins, many patients remain above goal and are at elevated risk for fatal and non-fatal CHD events. Objective: To project the impact of ezetimibe 10mg co-administration for typical CHD patients not attaining LDL-C goal (100 mg/dL or less) with current statin therapy in Germany. Method: From a retrospective study conducted in 62 practices across Germany, 339 CHD patients not at goal while on statin therapy were identified. Clinical trial data on the distribution of raw LDL-C changes was used to project the percent of patients who would reach LDL-C goal with ezetimibe 10mg added to their current statin therapy compared to current statin titration practice and to titration up to the maximum approved dose to reach goal. The impact of LDL-C changes on life expectancy was projected using Framingham risk equations and non-coronary mortality rates in Germany. Results: The mean age of the CHD cohort not at goal with current statin therapy was 64 years and 63% were men. Their statin therapies were atorvastatin (n=143), simvastatin (n=107), pravastatin (n=34), fluvastatin (n=29) and lovastatin (n=26). Mean LDL-C level was 150 mg/dL. Projected life expectancy with current statin dose was 14.2 years. Projected incremental benefits were reported in table 1.

Table 1: Projected Incremental Benefits Under Different Treatment Scenarios

	Titrate Statin According to Current Practice (11% of patients)	Titrate Statin up to Maximum Approved Dose to Reach Goal	Ezetimibe 10mg Co-administration
Incremental LDL-C Reduction	0.9%	15.3%	26.7%
Additional Patients at LDL-C Goal per 100 treated	1.3	29.5	44.3
Average Life-Years Gained per Patient	0.02	0.41	0.77

Conclusion: The typical German CHD patient not at LDL-C goal with current statin therapy is projected to benefit more with the co-administration of ezetimibe 10mg compared to either current statin practice or aggressive titration up to the maximum approved statin dose.

COST EFFECTIVENESS OF EZETIMIBE CO-ADMINISTRATION IN CHD PATIENTS NOT AT GOAL WITH ATORVASTATIN OR SIMVASTATIN THERAPY IN AUSTRIA

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Background: While treatment guidelines recommend lowering cholesterol to target levels appropriate for patients with existing CHD, many remain above their target even with the use of statins. Published clinical trial showed that ezetimibe (EZ) co-administration with existing statin therapy got 72% of patients to NCEP II goal versus 19% among patients continuing existing therapy. **Objective:** Assess the cost-effectiveness of EZ 10mg (EZ10) co-administration in CHD patients currently treated with Simvastatin or Atorvastatin and not attaining cholesterol goal (LDL-C 100 mg/dl).**Method:** Decision analytic model with discrete health states is used. Movement among health states depends on risk of recurrent CHD events based on Framingham Heart Study risk equations and nonCHD related mortality rates in Austria. Treatment strategies alter disease progression through LDL-C reductions as observed in clinical trials. The cost per life year saved (C/LY) is estimated for EZ10 co-administration compared to two statin alone strategies: 1)current statin dose is maintained (status quo) 2)statin dose is titrated (aggressive statin titration). The evaluations are conducted for 211 CHD patient profiles not at LDL goal on statin therapy (91 on Simvastatin and 120 on Atorvastatin). **Results:** The mean age of the 211 patients' is 62 years, 67% are men, and average LDL-C is 149 mg/dL while on statin therapy. EZ10 co-administration with atorvastatin is projected to increase life expectancy by 0.84 yrs compared to atorvastatin status quo and the incremental discounted C/LY is 15,926 EUR. Compared to a treatment strategy where all patients with a LDL-C > 100 mg/dL are titrated to maximum atorvastatin dose if necessary EZ10 co-administration with atorvastatin increases average life expectancy by 0.33 years and reduces total direct cost by 90,435 EUR per patient (cost saving). Cost-effectiveness analysis were also conducted for EZ10 co-administration with simvastatin, the incremental cost-effectiveness ratios were 16,143 EUR and 15,618 EUR when EZ10 co-administration was compared to status quo and aggressive simvastatin statin titration strategies respectively. **Conclusion:** For patients not at recommended LDL-C goal Ezetimibe co-administration with atorvastatin or simvastatin offers a cost-effective alternative compared to current treatment and statin titration.

THE POTENTIAL BENEFITS OF GOAL ATTAINMENT IN CHD PATIENTS NOT AT LDL-C GOAL WITH CURRENT STATIN THERAPY IN GERMANY

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Background: In Germany, treatment guidelines recommend LDL-C levels of less than 100 mg/dL and HDL-C levels of higher than 40 mg/dL for CHD patients. Even with statins, many patients remain above goal and are at elevated risk for fatal and non-fatal CHD events.
Objective: To project the potential life-year gains by getting all patients to their LDL and HDL-C goals.
Method: From a cohort study conducted in 62 practices across Germany, 339 CHD patients not at LDL-C goal while on statin therapy were identified. Their life expectancies under current therapies were projected using Framingham risk equations and non-coronary mortality rates in Germany. A second projection using the same method was also performed under the assumption that all patients had a LDL-C level of less than 100 mg/dL and a HDL-C level of greater than 40 mg/dL. The projected mean life-expectancies were compared to estimate the potential gains in life-expectancy by getting all patients to goal.
Results: The mean age of the CHD cohort not at goal with current statin therapy was 64 years and 63% were men. Their statin therapies were atorvastatin (n=143), simvastatin (n=107), pravastatin (n=34), fluvastatin (n=29) and lovastatin (n=26). Mean LDL-C and HDL-C levels on statin therapy were 150 mg/dL and 48 mg/dL, respectively. Projected life expectancy with current statin dose was 14.2 years. If all patients achieve their LDL-C and HDL-C goals, the projected life-expectancy would be increased to 15.3 years. The projected total life-years gained through goal attainment in this cohort of 339 CHD patients are estimated to be 365 years.
Conclusion: Helping CHD patients in Germany, who are on a statin but not at LDL-C goal, achieve their goals is projected to increase about one year of life per patient. The treatment guidelines bear substantial survival benefit.

PREVALENCE OF LOW HDL-CHOLESTEROL IN PATIENTS WITH CARDIOVASCULAR RISK FACTORS : THE ECHOS FRENCH SURVEY.

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The aim of this French Survey was to evaluate the prevalence of low HDL cholesterol - an important risk factor for cardiovascular disease (CVD) - in patients with cardiovascular (CV) risk factors. From October 2003 to February 2004, 1980 general practitioners recruited 5232 patients presenting with at least 2 items among the following: abdominal obesity, type 2 diabetes, hypertension, hypercholesterolemia (HC), hypertriglyceridemia (HTG) or a history of CVD. The overall population was 60.9 ± 10.7 yrs old, predominantly male (63.9%) with a mean BMI of 28.4 ± 4.6 kg/m^2 and a waist circumference of 100.1 ± 14.3 cm. Risk factors were distributed as follow: HC: 86.4% (with HTG: 56%), hypertension: 73.5%, abdominal obesity: 56.1%, diabetes: 32.9% and CVD history: 26.6%. 90% of the overall population had a recent (< 1 yr) dosage of HDL cholesterol, which had been performed under lipid lowering therapy (LLT) in 68.4% of the cases. Mean corresponding HDL cholesterol values were 53 ± 18 mg/dL in the overall population (n= 4688) and 48 ± 17 mg/dL when performed before any LLT (n=1655). Prevalence of low HDL in the overall population differs greatly according to the definition in use: from 8.7% if < 35 mg/dL to 19.1% if < 40 mg/dL and to 26.9% according to NCEP sex cut-off values (ie < 50 mg/dL in female and < 40 mg/dL in male, respectively). Prevalence of low HDL cholesterol was significantly higher in patients with HTG (OR 2.20, CI 1.76-2.75) p < 0.001, followed by abdominal obesity (OR 1.46 CI 1.19-181) p < 0.001 and diabetes (OR 1.36 CI 1.10-1.67) p=0.004, while there was no difference in patients with/or without hypertension and with/or without HC. Patients with CVD history tended to have a higher prevalence (OR 1.22 CI 0.98-1.52) p=0.07. There was a nice gradation of the low-HDL prevalence (< 35mg/dL) with the number of risk items present, from 6.2% with 2 items (n= 1399) (and 14.3% < 40 mg/dL), 7.6% with 3 items (n=1716) and to 11.2% with 4 or more items (n= 2117) (or 23.5% < 40 mg/dL) p < 0.001. Neither abdominal obesity (OR 1.10; CI 0.92-1.3), nor diabetes (1.07 CI 0.88-1.29) were linked to more frequent dosage of HDL cholesterol, while there are the most significant items associated with low HDL values.
In conclusion, this large survey shows the importance of concomitant risk factors on the prevalence of low HDL cholesterol, the highest prevalence being associated with obesity/HTG.

NEED FOR BETTER IMPLEMENTATION OF NATIONAL GUIDELINES FOR THE MANAGEMENT OF DYSLIPIDAEMIA IN FRANCE – EXAMPLE OF CURRENT ATORVASTATIN USE.

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The objective of this retrospective survey (GAMME, Global Atorvastatin Medical Management Evaluation) was to evaluate the implementation of French national guidelines for the management of dyslipidemia by evaluating the current use of atorvastatin. Data were collected from 6135 patients (mean age 61.7 years) treated with atorvastatin as either an initiation therapy (group 1, n=1475) or a switch therapy (group 2, n=4660). In the whole population, the atorvastatin treatment was initiated at 10mg (73%), 20mg (12%), 40mg (15%) and 80mg (0,4%) (mean dose : 16 ± 11mg).. The attainment of the LDL-cholesterol (LDL-C) goals recommended by French guidelines was determined for each atorvastatin dose in the global population and in groups 1 and 2: as a whole, 75% of patients had reached the LDL-C target (79% with atorvastatin 10mg, 68% with 20mg, 69% with 40mg, 44% with 80mg). The percentages of patients reaching the LDL-C goals were 66% in the sub-group of patients with coronary heart disease (CHD) and 78% in the sub-group without CHD. The initial dose of atorvastatin was maintained for 92% of patients. In the group of patients not reaching a goal, the dose of atorvastatin was increased for only 16% of patients. Single alanine aminotransferase elevations greater than 3 times the upper limit of normal range were noted in less than 1% of patients. The dosage of creatine phosphokinase values was prescribed for 31% of patients (n=1900): only 1 patient had a CPK elevation greater than 5 times the upper limit of normal. This French survey indicates that for patients not reaching the LDL-C goals, despite the excellent safety profile, the dose titration of atorvastatin (10mg to 80mg) adapted to patient's global cardiovascular risk profile was rarely realized underlying the insufficient implementation of dyslipidemia management guidelines in French primary care setting.

ACHIEVE CHOLESTEROL TARGETS FAST WITH ATORVASTATIN STRATIFIED TITRATION: A SUB-STUDY OF ACTFAST ON C-REACTIVE PROTEIN

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Background: C-reactive protein (CRP) is thought to participate in the development of atherosclerosis and eventual plaque rupture, and is a good predictor of cardiovascular events. Atorvastatin decreases CRP in various patient populations, but the dose-response relationship has not been elucidated.
Methods: ACTFAST is a 12-week, prospective, parallel arm, open-label trial which enrolled high risk subjects (either statin-free (SF) or statin-treated (ST) at baseline) with CHD or CHD-equivalent or a 10-year CHD risk >20%. Subjects with LDL >100 mg/dL but 220 mg/dL and triglycerides 600 mg/dL were assigned a starting dose of atorvastatin (10-80 mg/d) based on LDL and status of statin use at screening. After 6 weeks, where possible, subjects not reaching LDL target had their dose doubled. Blood was sampled at baseline, 6 and 12 weeks. Results are reported based on the intent to treat (ITT) and post-hoc per protocol (PP) populations. The post-hoc PP population is defined as ITT excluding subjects: 1) with a baseline hsCRP >10mg/L, 2) with an acute infectious episode or trauma and 3) using anti-inflammatory drugs during the study.
Preliminary results: The mean hsCRP concentration at baseline was 2.81 mg/L (95%CI: 2.69-2.94). Results (last observation carried forward) in SF subjects:

	ITT population (n=1343)		Post-hoc PP population (n=986)	
Dose	Δ hsCRP	95% CI	Δ hsCRP	95% CI
10 mg	-21%	-15 to -26%	-9%	-3 to -15%
20 mg	-28%	-19 to -36%	-24%	-13 to -34%
40 mg	-23%	-12 to -33%	-18%	-5 to -29%
80 mg	-34%	-27 to -40%	-30%	-23 to -37%

Interestingly, in ST subjects, atorvastatin 20-80mg provided an additional 12-17% reduction in hsCRP over that provided by the statin used at baseline (mean -13%; 95%CI: -7 to -18%).
Conclusion:
We observed a significant difference in the reduction of hsCRP between the 10 and 80 mg doses of atorvastatin when administered to SF subjects. This suggests that additional pleiotropic benefits may be obtained with more intensive lipid lowering therapy.

ACHIEVE CHOLESTEROL TARGETS FAST WITH ATORVASTATIN STRATIFIED TITRATION: THE ACTFAST STUDY

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Background: Many high risk patients do not achieve lipid targets defined in guidelines. This care gap may be explained by initiation of statins at an insufficient starting dose and/or by the lack of subsequent uptitration. An approach based on matching the starting dose of statin to the baseline LDL-cholesterol value and to the 10-year coronary heart disease (CHD) risk level may facilitate achievement of targets. The objective of the ACTFAST study is to validate such an approach.
Methods: ACTFAST is a 12-week, prospective, parallel arm, open-label trial which enrolled high risk subjects (either statin-free (SF) or statin-treated (ST) at baseline) with CHD or CHD-equivalent (diabetes, peripheral vascular disease or cerebrovascular disease) or a 10-year CHD risk >20%. Subjects with LDL >100 mg/dL but 220 mg/dL and triglycerides 600 mg/dL were assigned a starting dose of atorvastatin (10-80 mg/d) based on LDL and status of statin use at screening. After 6 weeks, where possible, subjects not reaching LDL target had their dose doubled. The primary endpoint was the proportion of subjects reaching a LDL target of <100 mg/dL.
Preliminary results: A total of 2114 subjects (64% SF) were enrolled in Canada, Italy, Spain and the UK. CHD, diabetes and other CHD-equivalents were present in 62%, 39% and 18% of subjects, respectively. At baseline, 32%, 37%, 11% and 20% of subjects were assigned to 10, 20, 40 and 80 mg, respectively. At 12 weeks, 80% of SF subjects reached LDL target (82%, 82%, 82% and 72% with 10, 20, 40 and 80 mg, respectively) and 59% of ST subjects achieved target (60%, 62% and 50% with 20, 40 and 80 mg, respectively). Interestingly, in the ST group, atorvastatin 20-80mg provided an additional 21%-42% reduction in LDL over the statin used at baseline. The proportion of subjects with severe adverse events was low and did not appear dose-related. The incidence of AST/ALT greater than 3 times and CK greater than 10 times the upper limit of normal were 1.2% and 0.05%, respectively.
Conclusion: This study confirms that the use of a flexible starting dose of atorvastatin allows the large majority of high-risk subjects to achieve their LDL target safely with the initial dose or with a single titration. The results provide clinicians with a simple algorithm for managing high-risk patients.

DISCOVERY: A COMPARISON OF EFFICACY AND SAFETY OF ROSUVASTATIN AND ATORVASTATIN IN HIGH-RISK SUBJECTS WITH HYPERCHOLESTEROLAEMIA

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In clinical practice, many patients fail to achieve lipid levels recommended by guidelines for the prevention of coronary heart disease. Consequently, more effective lipid-modifying therapies are required. DISCOVERY was a 12-week, parallel-group, open-label, randomised, multi-centre study comparing rosuvastatin (RSV) with atorvastatin (ATV) on changes in lipid levels and the achievement of European lipid goals. Patients (18 years) with high cardiovascular risk and LDL-C levels >3.5 mmol/l from primary care practices and hospital centres were randomised (2:1) to receive treatment with RSV 10 mg/day (n=627) or ATV 10 mg/day (n=284). Statin-naïve subjects had a 6-week dietary period before randomisation, whereas patients with LDL-C >3.1 mmol/l on another statin treatment were switched to the study drug immediately. Lipid levels were assessed at baseline and after 12 weeks. Baseline lipid levels and patient demographics were similar between treatment groups. More patients achieved LDL-C goals with RSV compared with ATV (Table). Both agents were well tolerated. RSV (10 mg/day) treatment for 12 weeks was significantly more effective than ATV (10 mg/day) at lowering LDL-C and enabled more patients in a high-risk primary care population to achieve recommended lipid goals.

	Mean change in LDL-C from baseline (%)†	Patients at LDL-C goal (%)	
		1998 European goals (<3 mmol/l)	2003 European goals (<2.5 mmol/l)
RSV (10 mg/day)	–48.6	83.4	73.2
ATV (10 mg/day)	–40.6*	68.3**	52.5**

*p<0.05 vs RSV, **p<0.001 vs RSV, †Statin-naïve patients only (n=761)

DIET AND THE RISE AND FALL OF CARDIOVASCULAR DISEASE MORTALITY IN NORWAY

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Background. Cardiovascular disease mortality in Norway during the last 50 years has been analyzed and related to changes in dietary habits and serum cholesterol in the population.
Material and methods. Mortality and dietary data have been collected from official statistics. Changes in serum cholesterol have been estimated from changes in intake of fatty acids based on published regression equations. Data on changes in serum cholesterol and blood pressure are from the former National Health Screening Service.
Results. Mortality from ischemic heart disease (IHD) peaked in 1966-70 when it was 100% higher than in 1951-55 for men and 50% higher for women. For age group 40-69 years mortality has been reduced by one half during the last 30 years. Mortality from sudden death has followed the same pattern as for IHD. Cerebrovascular disease mortality has shown a declining tendency during the entire period. Since 1960 the proportion of total fat in the diet has been reduced from 41 to 34 % of energy and the proportion of unsaturated to saturated + trans fatty acids has increased. Cholesterol in the diet has been reduced by almost one half. Based on changes in consumption in milk fat, fat from meat and margarine and taken into consideration the shift from boiled to filtered coffee the estimated reduction in serum cholesterol in the population is of the order of 0.8 mmol/l. The observed decrease is 0.5 to 1 mmol/l. Most of the reduction is due to changes in milk fat and margarine consumption and composition.
Interpretation. Based on the established relation between serum cholesterol and risk of IHD we conclude that reduction in serum cholesterol may explain most of the decline in mortality since 1970. Other factors that may have contributed are reduced smoking (in men), a small reduction in blood pressure, increased consumption of fruit, vegetables, cod liver – and fish oil and better means of treatment.

ASSESSMENT OF LIPID LOWERING DRUG TREATMENT IN GREECE

(RESULTS FROM A MULTI-CENTER OBSERVATIONAL STUDY)

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*Coordinator of the Study, Director of the 4th Department of Internal Medicine and Unit of Medical Angiology, " EVANGELISMOS" General Hospital, Athens, Greece.

Objective: To determine the percentage of subjects on lipid lowering drug treatment (LLDT) who achieve low-density lipoprotein cholesterol (LDL-C) goals as defined by the National Cholesterol Education Program (NCEP-ATP III) guidelines.
Methods: Adult patients with dyslipidemia, who had been receiving LLDT for at least 3 months, were assessed in a multi-center observational study performed at 70 investigational sites. Lipid levels were recorded prior to LLDT and at the end of the study period. The primary end point was the proportion of patients achieving their individual LDL-C target, according to coronary heart disease (CHD) risk status, as defined by NCEP guidelines.
Results: The study included 2,660 Greek adults (20-75 years) from 7 regions of Greece. Of the evaluable sample (n=2,211) 81% were on LLDT. From the subjects on LLDT 6% were at low CHD risk, 30% were at medium CHD risk and 63% had established CHD or equivalents (high risk). Overall, only 30% of patients on LLDT achieved NCEP-specified LDL-C target levels. Statins proved to be more effective than fibrates (p<0.0001). From the patients on statins those on atorvastatin (n=1,222, mean dose 18 mg/day) attained the target in 31% of the cases. This percentage was higher than that of patients receiving other LLDT (n=574, 26% on target, p=0.001). This outcome was more evident in the high CHD risk group (n=1,402, 26% on atorvastatin vs 16% on other LLDT attained LDL-C goal, ANOVA, p<0.0001).
Conclusions: The majority of dyslipidemic subjects receiving LLDT, and mainly those with high CHD risk, is not achieving the NCEP LDL-C target. This finding strongly suggests that a more aggressive approach (potent statins with dose titration) is needed in order to attain LDL –C goal, especially in patients with high risk for future cardiovascular events.

CONTROL OF DYSLIPIDEMIA IN OUT-PATIENT CLINICS IN GREECE

(RESULTS FROM A MULTI-CENTER OBSERVATIONAL STUDY)

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*Coordinator of the Study, Director of the 4th Department of Internal Medicine and Unit of Medical Angiology, " EVANGELISMOS" General Hospital, Athens, Greece.

Objective: To identify the characteristics of subjects on lipid lowering drug treatment (LLDT) and whether they are achieving treatment goals according to NCEP-ATP III guidelines.
Methods: A total of 2,660 Greek adults (20-75 years) with dyslipidemia, who had been on lifestyle advice and/or LLDT for at least 3 months in a primary or secondary care setting, were enrolled in the study. A post-treatment lipid analysis was performed and the relevant history was recorded. According to cardiovascular disease (CVD) risk category, subjects were considered to be at target for low-risk if they had LDL-C levels <160 mg/dl, for medium-risk (with 2 CVD risk factors but without CVD) LDL-C <130 mg/dl and for high–risk (with CVD or diabetes mellitus) if they had LDL-C <100 mg/dl.
Results: The patient population who had fasting lipid analysis (n=2,211, male 50,5%, mean age 62 ±9 years) is presented. Eighty-one percent were receiving LLDT (statins: 96% and fibrates: 3%) and 44% had a history of CVD; 61% had arterial hypertension, 36% diabetes and 26% first-degree family history of premature CVD. Six percent were at low, 30% at medium and 63% at high CVD risk. The percentage of subjects at LDL-C goal was: low risk 66.9% (95% CI=58.9-74.9), medium risk 29.3 % (95% CI=25.8-32.7) and high risk 19.8 % (95% CI=17.7-21.9).
Conclusions: The greater the CVD risk, the lower the percentage of subjects achieving target LDL-C levels by LLDT. This may be due, at least in part, to the low dose of hypolipidemic drugs being used, especially in higher CVD risk groups, who often necessitate a more aggressive LDL-C reduction regimen. Promoting healthy lifestyle and appropriate LLDT at effective dosages must be implemented in Greece to ensure that patients attain treatment goals and thus benefit by decreasing the individual CVD risk.

COST-EFFECTIVENESS OF LIPID-LOWERING AGENTS IN PATIENTS WITH MIXED HYPERLIPIDAEMIA IN DAILY PRACTICE IN POLAND.

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Objective: To define current practice patterns for patients with mixed hyperlipidaemia and to compare effects and costs of lipid-lowering agents in a naturalistic setting.
Methods: We analyzed retrospectively data on treatment patterns, clinical benefits and resource consumption in a cohort of patients with mixed hyperlipidaemia referred by their GPs to our institution for appropriate treatment. This cohort consists of patients referred by general practitioners after initial treatment failure. Patients were categorized into group [F] (initially receiving fibrates) and group [S] (initially receiving statins). The effectiveness in daily practice in terms of % change from baseline (CFB) in total cholesterol (TC): HDL-cholesterol ratio and achieving the NCEP ATP-II targets was assessed in each group at 12 months. The mean direct medical cost per patient per year in each group was calculated from health-care payers' perspective.
Results: A total of 409 patients were included: 254 in [F], 155 in [S]. Patients in group [F] had significantly higher baseline triglyceride levels, patients in group [S] - significantly higher baseline TC, LDL-C and HDL-C levels. Twenty six percent and 18% of patients in [F] and [S] respectively were switching from initial monotherapy to statin-fibrate combination. The % CFB of TC/HDL-C ratio in both groups was 30%. However, less than one sixth of the patients, especially those with the most severe hypercholesterolemia reached and sustained the NCEP ATP-II targets on treatment. The mean direct cost was 1467 PLN/patient/year in [S] and 935 PLN/patient/year in [F] (1 USD=4.0 PLN). The major cost driver was pharmaceuticals, approximately 2 times more expensive in [S] than in [F].
Conclusion: Although results from this study indicate that initial lipid lowering treatment for this cohort is in line with Polish clinical guidelines, the percentage of patients achieving guideline recommended goals is low in real-life, even in patients in [S] group. Starting therapy with fibrates provides similar effects in terms of % CFB in TC/HDL-C as starting the therapy with statins over 1 year and reduces medical costs from a health-care payers' perspective.

COST-EFFECTIVE SCREENING FOR METABOLIC SYNDROME IN PATIENTS TREATED WITH SECOND-GENERATION ANTIPSYCHOTIC DRUGS

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Despite concerns about the adverse effects of second-generation antipsychotics (SGA's) on lipid metabolism, glucose intolerance and weight regulation, little is known about the relationship between these agents and the metabolic syndrome. We assessed the prevalence of metabolic syndrome in a near-consecutive cohort of 89 newly admitted psychiatric inpatients treated with at least one SGS for various psychiatric disorders. Patients underwent measurements of lipid levels, fasting blood glucose, blood pressure, weight, height and waist circumference. Twenty-six of the 89 patients (29.2%) fulfilled criteria for the metabolic syndrome. Presence of the syndrome was associated with older age (p=.02), higher body mass index (p<.0001), and higher values for each individual criterion of the metabolic syndrome, but not with specific drugs or diagnoses. The presence of abdominal obesity was most sensitive (92%), while fasting glucose>110 mg/dl was most specific (95%) in correctly identifying the presence of metabolic syndrome. We conclude that the combined measurement of waist circumference and fasting blood glucose is a simple, cost-effective strategy to detect metabolic syndrome among psychiatric patients treated with drugs known to promote weight gain, dyslipidemia and insulin resistance.

THE ECONOMIC ASSESSMENT OF LIPID LOWERING THERAPY WITH EZETIMIBE CO-ADMINISTRATION IN A SWISS CHD PATIENT COHORT

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Background: Patients currently treated with statins in Switzerland remain above recommended goal (TC > 5 mmol/l). In a clinical trial, 72% patients receiving ezetimibe co-administered with existing statin therapy reached NCEP II goal versus 19% among patients continuing statin monotherapy. **Objective**: To assess cost-effectiveness of ezetimibe 10mg (EZ10) co-administration with simvastatin (SS) versus SS dose titration strategy in CHD and nonCHD diabetic patients not at cholesterol goal on SS monotherapy. **Method**: A decision-analytic model was developed to project lifetime costs and benefits of lipid therapy. Clinical trial data were used to estimate TC reductions for different treatment strategies. Effect of TC reductions on CHD event rates was estimated using Framingham equations and Swiss National Statistic data on nonCHD-related mortality. Direct costs of CHD events in Switzerland, Swiss prices for SS and EZ10 price were used to project lifetime costs. The model was run for a population of 111 patients who were currently on SS in an observational lipid lowering treatment study conducted in Switzerland, and had not reached goal during TC measurement at study end. **Results**: For these patients (mean age 68 years, 30% females, 86% CHD & 14% nonCHD diabetes patients, base TC 5.6 mmol/l), EZ10 co-administered with SS compared to SS titration is projected to increase life expectancy by 0.74 yrs (undiscounted) with a discounted C/LY of 19,360 CHF(12,521 EUR). The incremental cost per additional patient to goal in the first year was 1,516 CHF (985 EUR) per year. **Conclusion**: Based on the model, treatment with EZ10 co-administered with simvastatin for CHD or diabetic patients not at goal is a cost-effective alternative to simvastatin titration, well under the limit C/LY of 30,000 EURO considered acceptable in Switzerland.

THE ECONOMIC ASSESSMENT OF EZETIMIBE CO-ADMINISTRATION IN A HUNGARIAN CHD PATIENT COHORT

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Background: While current Hungarian guidelines recommend lowering cholesterol to target levels (TC >= 5 mmol/L), many remain above recommended goal. In a clinical trial, 72% of the patients who received ezetimibe (EZ) co-administered with existing statin therapy reached NCEP II goal versus 19% among patients who continued statin monotherapy. **Objective**: Access cost-effectiveness of EZ 10mg (EZ10) co-administration with atorvastatin (AT) versus AT dose titration strategy in CHD patients not at goal with AT monotherapy. **Method**: Decision-analytic model developed to project lifetime costs and benefits of lipid therapy. Clinical trial data were used to estimate TC reductions for different treatment strategies. Effect of TC reductions on CHD event rates was estimated using Framingham equations and Hungarian National data on nonCHD-related mortality. Direct costs of CHD events in Hungary, Hungarian prices for AT and EZ 10 price (based on German EZ10 price) were used to project lifetime costs. The model was run for a population of 48 patients treated with AT in an observational lipid lowering treatment study conducted in Hungary, and had not reached goal at the TC measurement after minimum 60 days of treatment. **Results**: For these patients (mean age 60.9 years, 50% male, lipid profile on AT; LDL-C 3.32 mmol/l, TC 6.0 mmol/l, HDL 1.44 mmol/l, triglycerides 2.79 mmol/l), EZ10 co-administered with atorvastatin compared to AT titration is projected to increase undiscounted life expectancy by 0.74 yrs with a discounted C/LY of 13,416 EURO and the discounted C/QALY's of 13,366 EURO. **Conclusion**: Treatment with EZ10 co-administered with AT for CHD patients not at goal is projected to be a more cost-effective alternative to atorvastatin titration and is substantially under the limit C/LY of 30,000 EURO.

INTRACEREBROVENTRICULAR NEUROPEPTIDE Y INFUSION PRECLUDES INHIBITION OF GLUCOSE AND VLDL PRODUCTION BY INSULIN.

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Recent evidence demonstrates that hypothalamic insulin signalling is required for inhibition of endogenous glucose production (EGP). The downstream mechanism responsible for the effects of hypothalamic insulin receptor activation on hepatic fuel flux remains to be established. Pro-opiomelanocortin (POMC) and neuropeptide Y (NPY) neurons in the arcuate nucleus are major targets of insulin in the brain, where it stimulates POMC neuronal activity and inhibits NPY neurons. To establish if downregulation of NPY release by insulin is mandatory for insulin's capacity to suppress glucose production, we examined the effects of a continuous intracerebroventricular (i.c.v.) infusion of NPY (10 µg/h for 3-5 hours) on glucose flux during a hyperinsulinemic euglycemic clamp. We also evaluated the effects of i.c.v. NPY administration on free fatty acid flux, glycerol flux and very low density lipoprotein production in this experimental context. In hyperinsulinemic conditions, the rate of glucose infusion necessary to maintain euglycemia was significantly decreased in NPY-infused mice compared to vehicle-infused animals (28.6 ± 8.6 vs. 59.8 ± 12.8 µmol/min/kg, P<0.01), which indicates that i.c.v. administration of NPY acutely induces insulin resistance. Peripheral glucose disposal in response to hyperinsulinemia was similar in vehicle- and NPY-infused animals. In contrast, hyperinsulinemia suppressed endogenous glucose production by approximately 30% vs. 8% in vehicle vs. NPY infused mice respectively (P<0.05). Glycerol and FFA turnover were not different in vehicle- vs. NPY-infused animals. However, VLDL-production was significantly higher during hyperinsulinemia in NPY- compared with vehicle-infused mice (97.5 ± 18.0 vs. 54.7 ± 14.9 µmol/kg/h, P < 0.01). These data show that i.c.v. administration of NPY precludes proper inhibition of glucose and VLDL production by circulating insulin, while it does not affect insulin-mediated fuel flux in other tissues. We infer that the neurophysiological action of insulin to downregulate hypothalamic NPY release is a prerequisite for its ability to suppress hepatic fuel production, whereas it is not mandatory for its capacity to modulate glucose dipsosal or lipolysis.

UNDERTREATMENT AMONG HIGH-RISK DYSLIPIDEMIC PATIENTS: RESULTS OF A NATIONAL SURVEY OF GOAL ACHIEVEMENT FOR NATIONAL CHOLESTEROL EDUCATION PROGRAM ADULT TREATMENT PANEL III GUIDELINES

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The Lipid Treatment Assessment Program, a national survey of physician compliance with National Cholesterol Education Program Adult Treatment Panel (NCEP ATP) guidelines (completed in 1997), showed significant underachievement of ATP II low-density lipoprotein cholesterol (LDL-C) goals. NCEP Evaluation ProjecT Utilizing Novel E-Technology (NEPTUNE) II was designed to estimate the probability of achieving NCEP ATP III cholesterol treatment goals in patients with treated dyslipidemia. A U.S. sample of very high prescribers of lipid-modifying medications (n=376: 83% primary care physicians; 17% cardiologists or endocrinologists) was asked to enroll 10 or 20 consecutive patients. Patient data were recorded using NEPTUNE II software on a Personal Digital Assistant and uploaded to a central database via the Internet. The number and percentage of patients in each risk category who achieved their LDL-C or LDL-C plus non-high-density lipoprotein cholesterol (non-HDL-C) treatment goals are shown below.

	0-1 Risk Factor	2+ Risk Factors	CHD + CHD RE[1]	Total
LDL-C Goal (mg/dL)	<160	<130	<100	--
Number of Patients	859	1318	2708	4885
% who Achieved LDL-C Goal (95% CI)	89 (86,91)	76 (73,78)	57 (55,58)	67 (66,69)
Non-HDL-C Goal (mg/dL)	<190	<160	<130	--
Number of Patients	163	340	728	1231
% who Achieved Both LDL-C and Non-HDL-C Goals (95% CI)[2]	64 (57,72)	52 (47,57)	27 (24,30)	39 (36,42)

[1]Coronary heart disease (CHD) and CHD risk equivalents (RE). [2]Goals in patients with triglycerides ≥200 mg/dL.

These results suggest improved compliance with LDL-C goals among very high prescribers of lipid-modifying therapies since 1997. However, a significant proportion of high-risk patients, especially those with elevated non-HDL-C due to hypertriglyceridemia, remain undertreated.

NUTRITIONAL ASSESSMENT FOLLOW – UP STUDY IN HAEMODIALYSIS PATIENTS

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In haemodialysed pts were frequently associated inflammation, malnutrition and atherosclerosis-MIA syndrom. Aim study was investigation with different methods 65 females (63,4 ± 8,2 years) and 46 males (61,3 ± 7,8 years) chronic haemodialysed pts cardiovascular risk and malnourished assessment.The serum transferrin levels were < 1,8 g/l in 63,72 % females,in 61,76 % males. The haematokrit was < 0,31 in 6,89 % females and 14,7 % mens.Prealbumin concentrations in females were in 18,97 % ,in males 29,11 % <199 mg/l.The albumin levels <8,01 g/l were in 15,52 % females ,in 29,41 % males. Total cholesterol levels decreased <4,5 mmol/l in 37,93 females , 58,82 % mens.The HDL-cholesterol concentrations were lower <1,4 mmol/l in 77,9 % females and 41,18 % mens. Hypertriglyceridaemia can be found in 41,38 % females , in 41,20 % males. CRP concentrations were higher >8,5 mg/l in 39 ,66 % females. In 50,01 % in males. The lymphocytes counts were smaller <18% in 29,31% vs 41,18% of females /mens .Subjective global assessment (SGA) measured moderate malnutrition in 56,01 % in females, and in 59,37 % of men, severe malnutrition (SGA-C) was in 20,01 % females and 9,38 % in mens. The bioimpedance analysis –with multifrequency analysis (inBody 3) was good correlation with decreased praealbumin ,albumin levels , LBW, increaased CRP and TBW parameters. The higher homocysteine levels (>25 umol/l) were in cerebro- and cardiovascular complications, non dipper hypertension, with high hyperbaric impact (419±124 mmHg/h), negative diurnal index. Malnutrition associated with low praealbumin, albumin, total and HDL cholesterol, high LDL, hypertriglyceridaemia, increased CRP concentration with high TBW, low BCM parameters with SGA-C stage.

CHANGE OF SERUM PARAOXONASE , OX – LDL ,TBARs CONCENTRATI - ONS AFTER FLUVASTATIN TREATMENT IN RENAL TRANSPLANTED PATIENTS

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Objective: Kidney transplanted patients have an increased risk of atherosclerosis, and lipidperoxidation, hyper-, et dyslipidaemia. The aim of our study investigated change of lipid levels and factors of lipid peroxidation after fluvastatin treatment. **Patients and Methods:** 21 men and 22 women (mean age 42,3±8,9 years) hyperlipidemic renal transplanted pts were treated with 40 mg/day fluvastatin. Authors determined total cholesterol (CHO), triglyceride, HDL, LDL-cholesterol and ApoA1 and ApoB lipids levels. They also monitored the change function of kidney, liver and paraoxonase (PON), nitric oxide (NO) activity, antibodies against of ox-LDL, homocysteine, cystatin C and TBARs concentrations. Blood pressure and cardiac events were registered with ABPM and ECG 24 hours monitoring (CardioTens-Meditech). **Results** :now after three months of fluvastatin treatment decreased significantly CHO, LDL and ApoB levels (p<0,001).Not change kidney and hepatic function. The PON activity increased 124±58 vs 121±75 U/L (n.s.), NO activity decreased siginificant (92,9±25,17 vs. 44,9±6,56 umol/l – p< 0,001), TBARs concentration decreased similarly significant 0,119±0,04 vs 0,085±0,026 umol/l, and ox-LDL concentration decreased 77,2±20,40 vs 64,9±17,4 U/l (n.s.).The homocysteine levels decreased not significant 15,46±5,21 vs. 14,93±4,72 umol/l and cystatin C concentrations were 2,29±0,61 vs. 1,85±0,47 mg/l. **Conclusions**: after fluvastatin treatment decreased lipidperoxidation, increased PON activity and decreased siginificant NO, TBARs and ox-LDL levels and improved endothel dysfunction. Blood pressure and cardiac events not significant decreased in time of fluvastatin treatment.

RELATIONSHIP BETWEEN SERUM PARAOXONASE ACTIVITY , POLYMORPHISM AND HOMOCYSTEINE CONCENTRATIONS IN HAEMODIALYSED AND TRANSPLANTED PATIENTS

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Introduction: In uraemic and kidney transplanted patients have an increased risk of atherosclerosis, increased lipoprotein oxidation. The serum paraoxonase (PON) is a HDL associated hydrolase ,which inhibits LDL oxidation. In uraemic, dialysed pts have hyperhomocysteinaemia ,which independent risk factor for accelerating atherosclerosis and cardiovascular complications. **Aims** our study determined serum paraoxonase activity, phenotype and dyslipidaemia with relationship homocysteine levels are renal transplanted, dialysed pts compare the values with healthy controls. **Patients and methods**: 110 healthy controls, 115 renal transplated (43,5±6,9 years) and 112 haemodialysed pts (61,3 ± 8,1 years) were in study. The PON activity determined spectrophotometry (412nm), PON phenotype with two substrate methods: paraoxonase and arylesterase ration was performed. The total homocysteine concentration determined with IMx (Abbott–kit) FPIA immunoassay method. **Results**: In kidney transplanted pts the concentrations of PON activity were higher than in dialysed pts. (121,10±78,76 vs. 87.35±54,72 U/L , $p < 0,01$). The different immunosuppressive treatment did not influence paraoxonase activity. In transplanted pts have high total and LDL cholesterol ,and ApoB levels ,in dialysed pts can be found the hypertriglyceridaemia ,with low concentrations HDL cholesterol and ApoAl levels. The hyperhomocysteinaemia were the highest in dialysed pts (25,52±6,71 umol/l - $p<0,01$) and the values of transplanted (15,46±5,02) and control (12,85±2,1 umol/l) pts were almost identical. The paraoxonase activity and homocysteine concentrations have negative correlation in dialysed and transplanted pts. The phenotypic distribution of paraoxonase in renal transplanted pts AA: 36 %, AB : 52 % ,BB :12 % vs in controll pts: AA: 41,44 % ,AB: 47,37 % ,BB: 11,18 % were. In haemodialysed pts were : AA. low activity homozygote : 66,67 % , moderate activity heterozygote AB: 31,62 % ,and high activity homozygote BB only :1,71 %! The standardized PON enzyme activity was lowest in dialysed pts. In control pts PON/ApoA1 was 103,29 ± 28,71 vs transplanted pts 79,15± 12,65 . **Conclusion** : The paraoxonase activity decreased in uraemic,dialysed pts and connection negativ correlation the homocysteine levels. After kidney transplantation significantly increased paraoxonase activity and decreased hyperhomocysteinaemia. In dyslipidaemic transplanted pts the low ratio of PON/HDL and PON/ApoAl may lead decreased antioxidant capacity of HDL than in healtly controls.