

Difficulties in reaching therapeutic goals for hypertension and dyslipidaemia in patients with type 2 diabetes in general practice

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ABSTRACT

INTRODUCTION: National guidelines recommend strict control of blood pressure (BP) and plasma low-density lipoprotein cholesterol (LDL) in type 2 diabetes (T2DM), aiming at a BP \leq 130/80 mmHg and a LDL concentration \leq 2.5 mmol/l. Angiotensin-converting enzyme inhibitors (ACEI) or angiotensin II-receptor blockers (ARB) are recommended as primary antihypertensive therapy (AHT). To which extent these targets are met in Danish primary care is unknown.

MATERIAL AND METHODS: This study was based on data from 2,057 patients with T2DM who were randomly selected from 64 general practitioners (GPs) from different regions of Denmark. Data were collected from the GPs' electronic records.

RESULTS: The mean age \pm standard deviation was 66.2 ± 11.6 years; 58.7% were male. The mean systolic BP \pm standard deviation was 132.6 ± 14.6 mmHg and the mean diastolic BP \pm standard deviation was 78.1 ± 9.0 mmHg. 47.7% of the patients met the BP target. 79.5% of the patients were on AHT. 55.1% of the untreated and 46.0% of the treated patients met the BP target. 83.4% of the treated patients received ACEI or ARB. The median LDL was 2.2 (1.7-2.7) mmol/l. 63.7% of the patients met the LDL target. 73.7% of the patients received lipid-lowering therapy. 32.8% of the untreated and 74.4% of the treated patients met the LDL target.

CONCLUSION: AHT including ACEI and ARB and lipid-lowering therapy are widely used in T2DM in Danish primary care, but only half of the patients are at target for BP and two thirds are at target for LDL. Increased use of diuretics may improve BP control.

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TRIAL REGISTRATION: not relevant.

Elevated arterial blood pressure (BP) is a major risk factor for the development and progression of micro- and macrovascular complications in patients with type 2 diabetes (T2DM) [1-3]. It is well-established that antihypertensive therapy, especially angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin-II receptor blockers (ARBs) have a beneficial effect on these compli-

cations [4-6]. Consequently, aggressive BP regulation is recommended in T2DM, aiming at a BP \leq 130/80 mmHg [7, 8].

The effect of lipid-lowering therapy, particularly statins, on macrovascular complications and mortality in T2DM is also well-documented [9, 10] and a concentration of plasma low-density lipoprotein cholesterol (LDL) \leq 2.5 mmol/l is currently recommended [7].

To meet these ambitious BP and LDL targets, Danish national guidelines recommend BP measurement at least four times annually and assessment of blood lipids at least annually in T2DM [7].

In hospital settings, data on BP, plasma lipid levels and medical treatment can be obtained from the National Indicator Project (NIP). However, only limited data on these important parameters are available for the majority of Danish patients with T2DM who are followed in primary care.

We have previously published on incomplete screening for microalbuminuria in Danish patients with T2DM followed in primary care [11]. The present sub-study reports on BP control, antihypertensive treatment, control of LDL and lipid-lowering therapy in these patients.

MATERIAL AND METHODS

The design of this observational study has been described previously [11]. The study included patients with T2DM for at least two years followed by 64 randomly selected GPs from different regions of Denmark, including both solo settings and group settings. GP practices were randomly recruited by telephone to ensure an even distribution of contacted GPs by region. Additional written information was sent to GPs willing to participate. At acceptance, the GPs applied for permission to participate from the Danish Health and Medicines Authority. In each GP's electronic patient records, all patients with T2DM were identified through a specific search for diabetes carried out by the GP in collaboration with a trained nurse. From this list, a median of 35 (interquartile range (IQR) 30-35) patients were randomly chosen and assigned a log number. From then on, only the GP had access to the patients' identity.

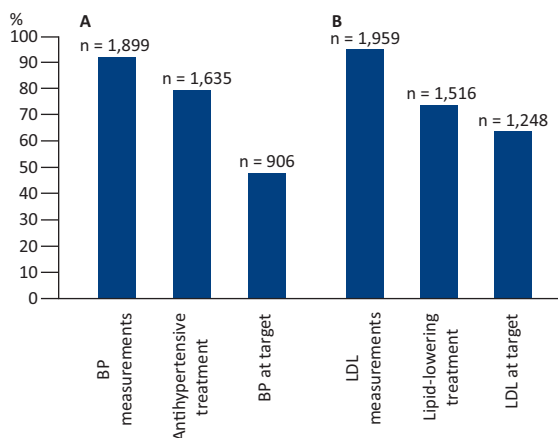
ORIGINAL ARTICLE

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FIGURE 1

A. Proportion of patients with type 2 diabetes with a measurement of blood pressure (BP) within the preceding 12 months, proportion receiving antihypertensive treatment, and proportion (of patients with a BP measurement) at target for BP ($\leq 130/80$ mmHg). **B.** Proportion of patients with type 2 diabetes with a measurement of low-density lipoprotein cholesterol (LDL) concentration within the preceding 12 months, proportion receiving lipid-lowering treatment, and proportion (of patients with measurement of LDL) at target for LDL concentration (≤ 2.5 mmol/l).



Primary and secondary endpoints

Our previous publication addressed another primary endpoint of the study: screening for microalbuminuria [11].

The pre-specified primary endpoint of the present sub-study was the proportion of patients meeting the targets for BP and LDL ($\leq 130/80$ mmHg and ≤ 2.5 mmol/l) with or without antihypertensive or statin treatment (Figure 1).

The secondary endpoints were classes of antihypertensive medication, particularly the proportion of patients treated with ACEI or ARB.

Other parameters

Standard clinical and laboratory characteristics of the patients including age, sex, duration of diabetes, history of cardiovascular disease (CVD), smoking, weight, body mass index (BMI), other pharmacological therapy (glucose-lowering and anticoagulant medication), and concentrations of the biochemical variables: HbA_{1c} and plasma-creatinine.

Statistical analyses

Statistical analyses were performed in collaboration with the Technical University of Denmark, which also hosts the database. Regardless of antihypertensive therapy, patients with a systolic BP ≤ 130 mmHg and a diastolic BP ≤ 80 mmHg were categorised as meeting the target BP. Similarly, patients with a LDL ≤ 2.5 mmol/l were cat-

egorised as meeting the LDL target. Data are presented as mean \pm standard deviation (normally distributed parameters) or median (IQR). Comparisons between groups were performed by Student's t-test (continuous variables) or χ^2 -test with Pearson's correction (discrete variables).

For non-normally distributed parameters, Wilcoxon's test or Fisher's exact test was applied. The study was approved by The Danish Data Protection Agency, and the participation of the GPs was approved by the Danish Medical Association.

Trial registration: not relevant, the project was non-interventional.

RESULTS

A total of 2,057 patients with T2DM were included. The mean age was 66.2 years, 58.7% were male and the median duration of diabetes was 5.0 years.

Lack of blood pressure measurement

A total of 158 patients (7.7%) had no BP measurement within the preceding 12 months. Such lack of data was more frequent for patients without antihypertensive therapy (59 of 422; 14.0%) than for treated patients (99 of 1,635 patients; 6.1%), $p < 0.01$.

Blood pressure control

Among all patients with BP measurements, the mean systolic BP was 132.6 ± 14.6 mmHg and the diastolic BP was 78.1 ± 9.0 mmHg. In total, 47.7% of the patients met the BP target ($\leq 130/80$ mmHg). In 25.6% of the patients, the diastolic but not the systolic BP was at target.

Antihypertensive therapy

79.5% of the patients were on antihypertensive therapy. Clinical and laboratory characteristics of treated versus untreated patients are given in Table 1.

The systolic BP was higher (133.5 ± 14.8 versus 129.0 ± 13.3 mmHg) in treated than in untreated patients ($p < 0.01$), whereas the diastolic BP was comparable between the two groups. 46.0% of the treated versus 55.0% of the untreated patients met the BP target ($p < 0.01$). Treated patients were older (67.3 ± 11.0 versus 61.7 ± 12.9 years, $p < 0.01$), had a longer duration of diabetes (5.0 (3.0-9.0) versus 4.0 (3.0-8.0) years, $p < 0.01$), and had a higher frequency of known CVD (22.3 versus 10.7%, $p < 0.01$) than untreated patients.

Moreover, the use of antihyperglycaemic agents (90.3 versus 83.9%), statins (76.6 versus 59.7%) and acetylsalicylic acid (51.0 versus 30.1%) was higher among patients on antihypertensive therapy than among untreated patients ($p < 0.01$ for all comparisons).



TABLE 1

Antihypertensive treatment: clinical and laboratory characteristics of study participants, subdivided according to antihypertensive therapy.

	All	Treated	Untreated	p-value ^a
Patients, n	2,057	1,635	422	—
Males, %	58.7	58.4	60.0	0.60
Age, years, mean ± SD	66.2 ± 11.6	67.3 ± 11.0	61.7 ± 12.9	< 0.01
Duration of diabetes, years, median (IQR); n	5.0 (3.0-8.5); 1,760	5.0 (3.0-9.0); 1,393	4.0 (3.0-8.0); 367	< 0.01
Active smokers, %	15.9	15.2	18.7	0.09
Antihyperglycaemic treatment, %	89.0	90.3	83.9	< 0.01
Antihyperglycaemic drugs received, n, median (IQR)	1.0 (1.0-2.0)	1.0 (1.0-2.0)	1.0 (1.0-2.0)	< 0.01
Metformin treatment, %	67.5	68.2	64.9	0.22
Insulin treatment, %	13.2	14.6	7.8	< 0.01
Antihypertensive drugs received, n, median (IQR)	—	2.0 (1.0-2.0)	—	—
Receiving ACEI and/or AIIA, %	—	83.4	—	—
Receiving ACEI and/or AIIA, diuretic and nothing more, %	—	21.0	—	—
Known cardiovascular disease, %	19.9	22.3	10.7	< 0.01
Statin treatment, %	73.1	76.6	59.7	< 0.01
Acetyl salicylic acid treatment, %	46.7	51.0	30.1	< 0.01
BMI, kg/m ² , mean ± SD; n	30.8 ± 5.8; 653	31.2 ± 5.8; 530	28.7 ± 5.7; 123	< 0.01
Systolic BP, mmHg, mean ± SD; n	132.6 ± 14.6; 1,899	133.5 ± 14.8; 1,536	129.0 ± 13.3; 363	< 0.01
Diastolic BP, mmHg, mean ± SD; n	78.1 ± 9.0; 1,899	78.0 ± 9.1; 1,536	78.2 ± 8.9; 363	0.81
BP, % at target; n	47.7; 1,899	46.0/54.0; 1,536	55.1/44.9; 363	< 0.01
Isolated systolic hypertension, %; n	25.6; 1,899	27.3; 1,536	18.5; 363	< 0.01
Plasma-creatinine concentration, normal/elevated/severely elevated, %; n	75.6/22.0/2.3; 2,008	73.4/23.9/2.7; 1,602	84.5/14.5/1.0; 406	< 0.01
Total cholesterol concentration, mmol/l, median (IQR); n	4.2 (3.7-4.7); 1,996	4.2 (3.7-4.7); 1,587	4.7 (3.7-5.2); 409	< 0.01
LDL concentration, mmol/l, median (IQR); n	2.2 (1.7-2.7); 1,959	2.2 (1.7-2.7); 1,561	2.2 (1.7-2.7); 398	< 0.01
HbA _{1c} concentration, %, median (IQR); n	6.7 (6.2-7.2); 1,722	6.7 (6.2-7.2); 1,386	6.7 (6.2-7.2); 336	0.20
GPs in solo practices, %	58.9	58.1	61.9	0.18
GPs in big cities, %	41.2	41.2	41.2	0.98

ACEI = angiotensin-converting enzyme inhibitors; AIIA = angiotensin II-receptor blockers; BMI = body mass index; BP = blood pressure; GP = general practitioner; IQR = interquartile range; LDL = low-density lipoprotein cholesterol; SD = standard deviation.

a) Student's t test, χ^2 -test, Wilcoxon's test, or Fisher's exact test, where appropriate, see Statistical analyses.

There was no sex difference between treated and untreated patients. Similarly, the proportion of patients on antihypertensive therapy did not differ between GPs in solo versus GPs in group settings or between GPs in big cities (> 100,000 inhabitants) with university hospitals versus GPs in smaller cities.

Angiotensin-converting enzyme inhibitors and angiotensin II-receptor blockers treatment

83.4% of the patients on antihypertensive therapy received an ACEI and/or ARB. The average number of antihypertensive agents was 2.0 (1.0-2.0). 21.0% of the treated patients received an ACEI or ARB combined with a diuretic drug.

Lack of low-density lipoprotein cholesterol measurement

A total of 56 patients (2.7%) had no plasma cholesterol measurement within the preceding 12 months. This was more frequent for patients without lipid-lowering therapy (26 of 541 patients; 4.8%) than for treated patients (30 of 1,516 patients; 2.0%) ($p < 0.01$).

Low-density lipoprotein cholesterol control

Among all patients with LDL measurements, the mean LDL was 2.2 (1.7-2.7) mmol/l. In total, 63.7% met the LDL target.

Lipid-lowering therapy

73.7% of the patients received lipid-lowering therapy; only four patients with other agents than statins. Clinical and laboratory characteristics of treated versus untreated patients are given in **Table 2**. The median LDL was higher in untreated patients (2.7; 2.2-3.2) than in treated patients (2.2; 1.7-2.7) ($p < 0.01$). 74.4% of treated versus 32.8% of untreated patients had an LDL at target ($p < 0.01$). The proportion of males was greater among treated than among untreated patients (60.4% versus 54.2% males, $p = 0.01$), whereas there was no age difference between these groups. Treated patients had a slightly longer duration of diabetes (5.0 (3.0-9.0) versus 5.0 (3.0-8.0) years, $p = 0.01$), and had a higher frequency of known CVD (23.2 versus 10.7%, $p < 0.01$) than untreated patients. Moreover, the use of antihyperglycaemic agents (91.6 versus 81.9%), antihypertensive ther-

TABLE 2

Lipid-lowering treatment: Clinical and laboratory characteristics of study participants, subdivided according to lipid-lowering therapy.

	All	Treated	Untreated	p-value ^a
Patients, n	2,057	1,516	541	—
Males, %	58.7	60.4	54.2	0.01
Age, years, mean ± SD	66.2 ± 11.6	66.1 ± 10.6	66.5 ± 14.0	0.53
Duration of diabetes, years, median (IQR); n	5.0 (3.0-8.5); 1,760	5.0 (3.0-9.0); 1,295	5.0 (3.0, 8.0); 465	0.01
Active smokers, %	15.9	16.8	13.5	0.09
Antihyperglycaemic treatment, %	89.0	91.6	81.9	< 0.01
Antihyperglycaemic drugs received, n, median (IQR)	1.0 (1.0-2.0)	1.0 (1.0-2.0)	1.0 (1.0-2.0)	< 0.01
Metformin treatment, %	67.5	69.7	61.4	< 0.01
Insulin treatment, %	13.2	13.9	11.1	0.11
Antihypertensive treatment, %	79.5	83.4	68.6	< 0.01
Antihypertensive drugs received, n, median (IQR)	1.0 (1.0-2.0)	2.0 (1.0-2.0)	1.0 (0.0-2.0)	< 0.01
Known cardiovascular disease, %	19.9	23.2	10.7	< 0.01
Acetyl salicylic acid treatment, %	46.7	54.0	26.4	< 0.01
BMI, kg/m ² , mean ± SD; n	30.8 ± 5.8; 653	30.8 ± 5.7; 521	30.4 ± 6.3; 132	0.41
Systolic BP, mmHg, mean ± SD; n	132.6 ± 14.6; 1,899	132.3 ± 14.3; 1,425	133.8 ± 15.5; 474	0.06
Diastolic BP, mmHg, mean ± SD; n	78.1 ± 9.0; 1,899	77.6 ± 8.9; 1,425	79.5 ± 9.4; 474	< 0.01
Plasma-creatinine concentration, normal/elevated/severely elevated, %; n	75.6/22.0/2.3; 2,008	74.8/22.6/2.6; 1,488	78.1/20.2/1.7; 520	0.28
Total cholesterol concentration, mmol/l, median (IQR); n	4.2 (3.7-4.7); 1,996	4.2 (3.7-4.7); 1,483	4.7 (4.2-5.7); 513	< 0.01
LDL concentration, mmol/l, median (IQR); n	2.2 (1.7-2.7); 1,959	2.2 (1.7-2.7); 1,456	2.7 (2.2-3.2); 503	< 0.01
LDL concentration < 2.0/2.0-2.4/≥ 2.5 mmol/l, %; n	39.0/24.7/36.3; 1,959	47.3/27.1/25.6; 1,456	14.9/17.9/67.2; 503	< 0.01
HbA _{1c} concentration, %, median (IQR); n	6.7 (6.2-7.2); 1,722	6.7 (6.2-7.2); 1,290	6.7 (6.2-7.2); 432	0.38
GPs in solo practices, %	58.9	59.4	57.5	0.48
GPs in big cities, %	41.2	41.8	39.4	0.35

BMI = body mass index; BP = blood pressure; GP = general practitioner; IQR = interquartile range; LDL = low-density lipoprotein cholesterol; SD = standard deviation.

a) Student's t test, χ^2 -test, Wilcoxon's test, or Fisher's exact test, where appropriate, see Statistical analyses.

apy (83.4 versus 68.6%) and acetylsalicylic acid (54.0 versus 26.4%) was higher among patients on lipid-lowering therapy than among untreated patients ($p < 0.01$ for all comparisons). There was no difference in the proportion of patients on lipid-lowering therapy between GPs in solo versus GPs in group settings or between GPs in big cities (> 100,000 inhabitants) with university hospitals versus GPs in smaller cities.

DISCUSSION

The main results of this study were that around half of the patients with T2DM in Danish primary care met the BP target of $\leq 130/80$ mmHg and almost two thirds of the patients met the LDL target of ≤ 2.5 mmol/l as set out in national Danish guidelines [7] Thus, recommended BP control seems to be particularly difficult to achieve in these patients who are at high risk of microvascular and cardiovascular complications.

The discrepancy between optimal control of BP and LDL may exist for several reasons. One explanation may be less awareness of the need for BP regulation than for LDL control. However, in the majority of patients, both the BP and the LDL had been measured within the preceding 12 months, although it should be noted that 7.7% had no BP measurement performed, whereas only 2.7%

lacked measurements of plasma lipids. Antihypertensive and lipid-lowering therapy was frequent, with 79.5% and 73.7% of the patients receiving this therapy. Thus, there seems to be good attention to both BP and lipid control.

Another factor that may explain the lower degree of optimal BP versus LDL control is that the LDL target is often achieved by a single drug, whereas a combination of several drugs is usually needed to achieve the BP target. Only 26% of the patients on lipid-lowering treatment had an LDL above the target level compared with 67% of untreated patients, which indicates that on-going statin treatment is an important determinant for control of the LDL in the present population of patients with relatively uncomplicated T2DM. These results are in accordance with those of a recent study by Siggaard-Andersen et al. in the Copenhagen General Population Study, which included 2,155 patients with diabetes [12]. In total, 48% of these diabetic patients received lipid-lowering therapy with a clearly increasing trend from 2004 through 2010. 71% of the untreated and 27% of the treated patients had an LDL > 2.5 mmol/l.

In contrast, although the median number of antihypertensive drugs was 2.0 per treated patient; only 46.0% of the treated patients were at target for BP [7, 8]. In the UKPDS, more than 60% of the patients needed two or

more antihypertensive agents to reach the much less ambitious goal of < 150/85 mmHg [4]. Although a direct comparison with the UKPDS is difficult, the present study confirms that reaching the BP target of $\leq 130/80$ mmHg is difficult. Also the Steno 2 trial in T2DM patients with microalbuminuria demonstrated that intensive BP control of < 130/80 mmHg was not achieved in all patients as intended [13]. Some patients may need combination therapy with three or more antihypertensive agents to reach optimal BP regulation and others may be treatment-resistant.

More pronounced adverse reactions for antihypertensive than for lipid-lowering drugs may also contribute to the lower frequency of achieving the BP than the LDL target. Some patients may therefore have stopped or reduced pharmacological treatment in agreement with their GP due to unacceptable side effects or intolerance. Unfortunately, we have no information on earlier intended treatment.

Finally, some patients or GPs may doubt the value of AHT and/or lipid-lowering treatment. Importantly, recent data question the benefit of achieving very low BP values in patients with T2DM [14, 15], and guidelines are accordingly under revision. Less use of guideline-based treatment could also be related to the sometimes severe co-morbidity among T2DM patients, but the study was not able to confirm this. We found no influence from GPs' solo versus group setting or urbanisation on the treatment pattern for antihypertensive drugs or statins.

In accordance with recommendations in T2DM, ACEIs and ARBs were widely used in the present study. 83.4% of the treated patients received this therapy which is presumably close to what is maximally achievable as some patients may have allergy or intolerance to these drugs. However, combined therapy of ACEI or ARB with a diuretic was only observed in 21.0% of the patients, although this is a generally recommended and effective combination.

A new Sentinel Data Capture system under implementation in Danish primary care will provide individual feedback quality reports for the GP on key data from patients with chronic diseases, including data on treatment of hypertension and dyslipidaemia and target achievement in patients with diabetes. It is unknown if this new modality will change the control of these crucial risk factors, but the system will allow for extraction of data at the national level for research purposes like the present.

The main strength of the present study is the large number of patients and clinics included, which allows for a statistically precise evaluation of the treatment of hypertension and lipids in T2DM in Danish primary care, as well as for statistical analysis of factors potentially related to GPs (size of practice and geography) or patients



Difficulties in reaching therapeutic goals for hypertension and dyslipidaemia in patients with type 2 diabetes in general practice.
Photo: Colourbox

(age, sex, co-morbidity, etc.) that could influence treatment intensity and target attainment. In addition, the primary-care-based design with inclusion of different types of GPs (solo/group) from all regions of Denmark strengthens the external validity of the study and minimises the risk of selection bias compared with studies on patients referred to secondary care settings. However, selection cannot be excluded. It might well be that GPs willing to participate in the present study are particularly interested in T2DM and, consequently, more likely to follow guidelines. Furthermore, it is possible that some GPs did not want to participate in the study because of sponsor support from the pharmaceutical industry. Selection might explain the observed small gender difference which is probably without any importance for the results of the study.

In conclusion, AHT including ACEI and ARB and lipid-lowering therapy are widely used in T2DM in Danish primary care, but only half of the patients meet the BP target and around two thirds meet the LDL cholesterol target. Increased use of diuretics might improve BP control.

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LITERATURE

1. Adler AI, Stratton IM, Neil HA et al. Association of systolic blood pressure with macrovascular and microvascular complications of type 2 diabetes (UKPDS 36): prospective observational study. *BMJ* 2000;321:412-9.
2. Knudsen ST, Laugesen E, Hansen KW et al. Ambulatory pulse pressure, decreased nocturnal blood pressure reduction and progression of nephropathy in type 2 diabetic patients. *Diabetologia* 2009;52:698-704.
3. Laugesen E, Rossen NB, Poulsen PL et al. Pulse pressure and systolic night-day ratio interact in prediction of macrovascular disease in patients with type 2 diabetes mellitus. *J Hum Hypertens* 2012;26:164-70.
4. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. UK Prospective Diabetes Study Group. *BMJ* 1998;317:703-13.
5. Effects of ramipril on cardiovascular and microvascular outcomes in people with diabetes mellitus: results of the HOPE study and MICRO-HOPE substudy. Heart Outcomes Prevention Evaluation Study Investigators. *Lancet* 2000;355:253-9.

6. Patel A, MacMahon S, Chalmers J et al. Effects of a fixed combination of perindopril and indapamide on macrovascular and microvascular outcomes in patients with type 2 diabetes mellitus (the ADVANCE trial): a randomised controlled trial. *Lancet* 2007;370:829-40.
7. Dansk Selskab for Almen Medicin. Type 2-diabetes i almen praksis. En evidensbaseret vejledning. www.dsam.dk/files/9/type_2_diabetes_2004_rettet.pdf (1 May 2012).
8. Mansia G, De BG, Dominiczak A et al. 2007 ESH-ESC Guidelines for the management of arterial hypertension: the task force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *Blood Press* 2007;16:135-232.
9. Jonsson B, Cook JR, Pedersen TR. The cost-effectiveness of lipid lowering in patients with diabetes: results from the 4S trial. *Diabetologia* 1999;42:1293-301.
10. Kearney PM, Blackwell L, Collins R et al. Efficacy of cholesterol-lowering therapy in 18,686 people with diabetes in 14 randomised trials of statins: a meta-analysis. *Lancet* 2008;371:117-25.
11. Knudsen ST, Mosbech TH, Hansen B et al. Screening for microalbuminuria in patients with type 2 diabetes is incomplete in general practice. *Dan Med J* 2012;59(9):A4502.
12. Siggaard-Andersen N, Freiberg JJ, Nordestgaard BG. Only a fraction of patients with ischaemic diseases or diabetes are treated to recommended target values for plasma lipids. *Dan Med J* 2012;59(7):A4470.
13. Gaede P, Vedel P, Parving HH et al. Intensified multifactorial intervention in patients with type 2 diabetes mellitus and microalbuminuria: the Steno type 2 randomised study. *Lancet* 1999;20;353:617-22.
14. Cushman WC, Evans GW, Byington RP et al. Effects of intensive blood-pressure control in type 2 diabetes mellitus. *N Engl J Med* 2010;362:1575-85.
15. Vamos EP, Harris M, Millett C et al. Association of systolic and diastolic blood pressure and all cause mortality in people with newly diagnosed type 2 diabetes: retrospective cohort study. *BMJ* 2012;345:e5567.