

Evidence-performance gap in primary care revisited in patients with diabetes

Original Article

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Abstract Evidence-performance-gaps between guidelines and treatment of type 2 diabetes (T2DM) in daily practice have been reported, especially in primary care. We aimed to assess the potential gap comparing current treatment in primary care with guidelines and patients' characteristics from large clinical trials that guidelines are based on, namely UKPDS, ACCORD, ADVANCE, STENO-2 and VADT. Methods: We undertook a cross-sectional study and extracted data on 541 patients with T2DM from a clinical information system of a GP network in Switzerland. Results: Our study population was comparable to patients in ACCORD, ADVANCE and VADT at baseline. Patients in UKPDS and STENO-2 differed in age and disease duration. HbA1c-levels (7.3%), LDL-level (2.6 mmol/l), systolic and diastolic (135/78 mmHg) blood pressure were lower in our study than in the reference studies. 39.4% received an ACE-inhibitor, 41.6% statins and 41.4% aspirin. Conclusion: Taking into consideration the results of recent large clinical trials indicating that very strict treatment goals are of no additional benefit, most patients in Swiss primary care would not benefit from a treatment intensification regarding HbA1c, blood pressure and cholesterol targets. Evidence-performance-gaps were observed mainly concerning the choice of first line medication.

Keywords diabetes, cardiovascular risk, primary care, guidelines, evidence-performance gap

1. Introduction

Guidelines and treatment recommendations are usually based on the results of large clinical trials. Regarding the treatment of cardiovascular risk factors in patients with type 2 diabetes (T2DM), the guideline of the European Society of Cardiology (ESC) and the European Association for the Study of Diabetes [1-3] target values for glycated haemoglobin (HbA1c), lipid-levels, blood-pressure and gives recommendations for ideal weight as well as pharmacotherapy. This guideline is accepted as a standard for clinical practice in Europe as well as in Switzerland. The latest version of these guidelines [2] recommends rather moderate target values and emphasizes the necessity of individualized treatment plans, taking into account age, duration of T2DM, history of cardiovascular disease (CVD) and other comorbidities. However, in the past, the recommended target values were very strict. Many studies have revealed a substantial gap between guidelines and treatment (evidence-performance-gap) in daily practice, especially in primary care [4-6]. One approach for explaining this evidence-performance-gap is to assume substantial differences between the patients included in the

large – mostly pharmaceutical – randomized controlled trials (RCTs) and the patients seen by general practitioners (GP) in daily practice. This approach is supported by a study of Boyd et al. outlining that 40% of clinical trials on diabetes excluded patients with comorbidities such as cardiovascular disease and 17% excluded patients aged >65 years [7]. Lacking guideline-adherence would be a consequence of the GPs' adaption of the target values to their "real life patients" and the individualization of treatment plans balancing benefits of stringent goals and their potential harms for patients of higher age, with multimorbid conditions or proneness to hypoglycaemia. An exploration of this hypothesis could be undertaken on the basis of a structured comparison between a population of GP patients with T2DM and the study populations of large clinical RCTs that contributed to the specification of target values. In this context, a description of patients with T2DM treated in Swiss primary care could be of international value, because Switzerland is a good example of a western country with an insurance based health care system with a fee-for-service reimbursement and mostly free choice of doctors – a model that can also be found in other countries, e.g. Austria, France or Germany. However, both data on the characteristics and on metabolic and cardiovascular risk control in Swiss GP patients with T2DM are scarce.

2. Objective

The aim of this study is to gather information on patients with long-standing T2DM in Swiss primary care and to assess a possible performance gap in comparing current treatment with guidelines under consideration of differences between these real life patients to patients from large clinical trials, namely UKPDS [8], ACCORD [9], ADVANCE [10], VADT [11] and STENO-2 [12].

3. Methods

Data on patients with T2DM were prospectively collected in a GP network in the greater region of Zurich (Medix), Switzerland, using an internet based clinical information system (DataBox), which enables the registration of vital parameters, laboratory values, actual medication, as well as the early detection of diabetic complications. There was no special standardization in terms of data acquisition throughout the participating practices. GPs were asked to include all patients with T2DM consecutively as they appeared in the practice. Patients with newly diagnosed diabetes mellitus (less than 6 months) were excluded from the analysis due to the study aim of investigating only patients suffering from long-standing diabetes. The

data presented in this study are from the last consultation of each patient during the period from January 2010 until April 2011.

We assessed sociodemographic parameters (age, sex, duration of disease), glycemic control (HbA1c), cardiovascular risk factors (systolic and diastolic blood pressure (BP), Low Density Lipoprotein (LDL)-cholesterol concentration, smoking behaviour, Body Mass Index), multimorbidity (diagnosis of chronic illness in addition to T2DM) and medication from the structured entries in the DataBox database.

Corresponding information about the study populations of UKPDS [8], ACCORD [9], ADVANCE [10], VADT [11] and STENO-2 [12] were retrieved from the original publications by two independent investigators (SD, FM). We compared our data with the baseline characteristics of the above-mentioned large landmark studies.

At the time that the study was conducted and patients in our study received care, the ESC/EASD guidelines of 2007 [1] were valid and defined target values for HbA1c, systolic and diastolic BP and LDL-cholesterol concentration. We measured our findings against these target values as well as against the target values proposed by the latest version of the guideline [2] and evaluated the potential evidence-performance gap.

3.1 Statistical analysis

Continuous variables are presented as means and standard deviations (SD), categorical data as frequencies and percentages. Data were analysed using Microsoft Excel 2010 software (version 14.0.6106.5005).

4. Results

Between January 2010 and April 2011 21 out of 92 eligible network GPs collected data on a total of 541 patients suffering from T2DM for more than 6 months. Patient characteristics are provided in table 1.

((Position of Table 1))

Table 1. Patient characteristics according to study population and ESC/EASD guideline. Data are presented as mean values \pm standard deviation if not otherwise declared (n.a = not available).

4.1 Sociodemographic parameters

Regarding the sociodemographic parameters the mean age of our study population was older (68 ± 12 years) than in UKPDS (53 ± 9 years), ACCORD (62 ± 7 years), ADVANCE (66 ± 6 years), STENO-2 (55 ± 7

years) and VADT (60±9 years). The proportion of female patients was 32% in our study, 39% in UKPDS, 39% in the ACCORD-study, 42% in the ADVANCE-trial and 26% in STENO-2. In the VADT-trial virtually all patients were male. The time since T2DM onset in our study was 10.3±7.8 years, this was similar in the ACCORD-study (10 years), while the duration of T2DM in the VADT-trial (11.5±8 years) was longer. Duration of disease was shorter in ADVANCE (8±6 years) and STENO-2 (6 years). The UKPDS-study only included patients with newly diagnosed type 2 diabetes.

4.2 Glycemic control

HbA1c was chosen as a surrogate for glycemic control. In our study population, HbA1c was 7.3±1.2% in 530 analyzed patients which is comparable to the ADVANCE-trial (7.2±1.6%) but less than in ACCORD (8.3±1.1%), STENO-2 (8.8±1.6%) and VADT 9.4±2.0%). HbA1c in the UKPDS-study was not directly comparable because patients had newly diagnosed T2DM.

The ESC/EASD guideline of 2007 cites international diabetes associations, recommending a HbA1c target of ≤6.5% or <7% [1]. In 2013, the guideline recommends a target value of ≤7% with acknowledgement of individual requirements of the patient. For elderly people in whom lower targets cannot be achieved, a HbA1c level of 7.5–8% is recommended [2].

4.3 Cardiovascular risk factors

Cardiovascular risk factors in addition to T2DM were defined as arterial hypertension, dyslipidemia, overweight/obesity and smoking. We had no information on familiar predisposition. The proportion of patients with one, two or three additional cardiovascular risk factors was 46%, 29% and 3% respectively. T2DM was the single reported cardiovascular risk factor in 22% of patients. The mean age of patients with T2DM as the only cardiovascular risk factor was 69.6±12.3 years, similar to the mean age of the whole study population.

Mean systolic BP in our study was 135±16 mmHg, which was similar to baseline measurements in UKPDS (135±20 mmHg), ACCORD (136±17 mmHg) and VADT (132±17 mmHg) and less than in ADVANCE (145±22 mmHg) and STENO-2 (149 mmHg). Mean diastolic BP was 78±10 mmHg. Thus, it was lower than in UKPDS (82±10 mmHg), ADVANCE (81±11 mmHg) and STENO-2 (86 mmHg) but higher than in ACCORD (75 mmHg) and VADT (76±10 mmHg).

The ESC/EASD guideline of 2007 [1] recommends a target value of <130/80 mmHg. Consequently, the

prevalence of hypertensive BP in our study population was 73% (452 of 541 patients analyzed). Considering the less stringent BP goals of the current guideline (<140/85 mmHg) [2] still 44.5% of our patients did not meet the criteria.

Laboratory data on lipid-concentrations were obtained in 350 out of 541 patients. The mean LDL level was 2.6±1.0 mmol/l and thus lower than in all landmark studies (table 1).

Both ESC/EASD guidelines of 2007 and 2011 recommend a LDL-cholesterol target value of <1.8 mmol/l for patients at very high cardiovascular risk (documented or severe CVD, or ≥1 cardiovascular risk factor in addition to T2DM and/or target organ damage) and <2.5 mmol/l for patients with high cardiovascular risk (no cardiovascular risk factor in addition to T2DM and free of target organ damage) [1, 2]. In our study, 77% of the patients had a LDL level of ≥1.8 mmol/l and 53% had a LDL level >2.5 mmol/l.

Overweight, defined as a BMI of 25 kg/m² or more, was prevalent in 82% of our study population. The prevalence of obesity defined as a BMI of 30 kg/m² or more was 42% in our study (400 of 541 patients analyzed). Although the mean BMI of our study population (29±5 kg/m²) was higher than in the UKPDS-trial (28±5 kg/m²) and ADVANCE-trial (28±5 kg/m²), it was lower than in ACCORD (32±6 kg/m²), STENO-2 (31 kg/m²) and VADT (31±4 kg/m²).

Treatment goals according to the ESC/EASD guideline are defined as BMI<25 kg/m². The latest guideline drops specific thresholds and suggests weight stabilization based on calorie balance as a goal.

The proportion of current smokers was 7%, the lowest in our study compared to the landmark trials. The UKPDS-trial reported 30% current smokers, the ACCORD- and ADVANCE-trial reported 14% current smokers each, while in the STENO-2-study there was a proportion of 38% current smokers and 17% in the VADT-trial.

4.4 Multimorbidity

In a subset of 350 patients information on multimorbidity was available.

Multimorbidity, defined as at least one chronic condition (arterial hypertension, coronary heart disease, obesity, chronic obstructive lung disease, asthma, chronic renal insufficiency or depression) in addition to T2DM was prevalent in 81% of these patients. 13% of our study population had a history of coronary heart disease compared to 40% in VADT, 37.5% in STENO-2, 35% in ACCORD and 32% in ADVANCE. UKPDS did not provide respective information. Availability of further data on comorbidity was varying across the reference

trials and therefore was not directly comparable with our study.

4.5 Medication

Information on medication was available in all of the 541 patients. Only the ADVANCE-trial and the STENO-2-study provided similarly comprehensive data on medication use. An overview about the medication is provided in table 2.

((Position of Table 2))

Table 2. Medical treatment according to study population. Data are presented as % if not otherwise declared (n.a = not available).

Metformin was the most prescribed antidiabetic drug in 58.6% of our patients. This was lower than in ADVANCE but higher than in STENO-2. Sulfonylurea was taken by 26.4% in our study, which was less than in both ADVANCE (63.5%) and STENO-2 (54.5%). Insulin was used by 16.1% of our patients, which was less often than in ACCORD (35.0%) and VADT (52.0%) but more than in ADVANCE (11.5%) and STENO-2 (10.0%). Both, the ESC/EASD guideline of 2007 and 2011 recommend metformin as first-line agent in patients with T2DM especially when overweight.

39.4% patients of our study population received an angiotensin-converting-enzyme (ACE)-inhibitor. This proportion was lower than in the ACCORD-study. 54.2% of our patients took either an ACE-inhibitor and/or an angiotensin-II-receptor (ATII)-antagonist, which was more than in the STENO-2-trial (19.5%). 7.9% received other antihypertensive drugs. Both, the ESC/EASD guideline of 2007 and 2011 recommend ACE-inhibitors as first-line antihypertensive drug in patients with T2DM.

Aspirin was prescribed in 41.4% of cases in our study as compared to 44.0% in ADVANCE and 14.0% in STENO-2. Both ESC/EASD guidelines recommend aspirin as secondary prevention in patients with T2DM but not as primary prevention. Statin use was only higher in the ACCORD-trial (59.3%) while statins were prescribed in 41.6% of our study population, 28.3% in ADVANCE and 1.5% in STENO-2 respectively. 86 of 235 (37%) patients in our study population with an LDL-cholesterol concentration of 1.8 mmol/l and higher were prescribed a statin, while 38 of 70 (54%) patients with a LDL concentration of less than 1.8 mmol/l were taking a statin. Of those patients with a history of CVD, 35.7% received a statin. The ESC/EASD guidelines of 2007 recommend a statin therapy for all patients with T2DM but without CVD if the total cholesterol level is >3.5 mmol/l, whereas patients with T2DM and CVD should receive statins regardless of LDL or total cholesterol

[1]. In contrast, the latest guidelines recommend statins in all patients with T2DM, only the treatment goal varies depending on the cardiovascular risk profile [2].

5. Discussion

In our study we analyzed the characteristics of patients with diabetes type 2 from general practices in the greater region of Zurich, Switzerland and compared them with baseline characteristics of the study populations from large landmark studies, namely UKPDS, ACCORD, ADVANCE, STENO-2 and VADT.

5.1 Differences between populations

Our results show that our study population is comparable to the populations described in the landmark studies, namely ACCORD, ADVANCE and VADT, especially as far as age, duration of T2DM, BP, LDL-levels and BMI is concerned. The proportion of smokers varied widely among the different trials, being the smallest in our study. These differences are probably due to inconsistent data recording, therefore the prevalence was regarded as not directly comparable. Also, information on comorbidities was scarcely reported by the landmark studies and thus not directly comparable. However, it is to note, that the range of additional cardiovascular risk factors other than T2DM was greater in our study than reported by the other studies (1–4 factors vs. at least 1 factor).

The study population in UKPDS was clearly younger, included only patients with newly diagnosed T2DM with lower HbA1c values, lower BMI and higher mean LDL. In the STENO-2-trial, besides a relatively young age at baseline, HbA1c, BP and LDL-levels were among the highest compared to the other studies. The difference in patient characteristics between our study population and the UKPDS and STENO-2-trial is explained by strict exclusion criteria in the process of patient recruitment in these studies. In contrast, our study population represents a real life setting since patients were included consecutively during daily consultations in general practice. To conclude, populations in ACCORD, ADVANCE and VADT were more similar to a real life population in Swiss primary care than the population in UKPDS and STENO-2. As a consequence, recommendations retrieved from these studies are more likely applicable to primary care than are recommendations retrieved from the latter studies. In spite of the comparability with ACCORD, ADVANCE and VADT at first sight, HbA1c, BP and LDL-concentration in our study were the lowest compared to the other trials at baseline. We explain

this finding with the influence that these landmark studies generally had on physicians' awareness on diabetes care and cardiovascular risks and led them to intensify their treatment on the one hand, but at a slower rate and with less aggressive goals than imposed by the ESC/EASD guidelines of 2007, valid at the time that the study was conducted. Thus, only a minority of patients in our study achieved the stringent target values of this guideline.

5.2 Gaps in comparison to guidelines

With respect to glucose control, the 2007 ESC/EASD guidelines for treating diabetes mainly rely on evidence from the UKPDS- and STENO-2 trial [1]. In both studies gaps between patient characteristics compared to our study were the largest. In the ACCORD-study, where patient characteristics were closer to our study population, an increased mortality with tight blood sugar control could be demonstrated [9, 13].

Regarding BP, the stringent goals as proposed by the ESC/EASD guidelines 2007, are mainly based on the UKPDS-study [14] and the HOT-study [15]. Both studies show substantial differences with respect to baseline characteristics compared to our study population, especially age. Evidence for lowering BP below 130/80 mmHg in patients with T2DM comes mainly from the ACCORD BP-trial [16], the SANDS- [17] and the ABCD-trial [18]. While the ACCORD-BP-trial and the ABCD-trial showed a benefit of stringent BP control regarding stroke and progression of proteinuria, neither the ACCORD-BP-trial nor the ABCD-trial or the SANDS-trial could show a benefit in reduction of coronary risk. Instead a common finding of all three studies was a rise in adverse events related to antihypertensive therapy.

Regarding lipid lowering therapies current evidence shows a reduction of cardiovascular risk in secondary prevention with statins while reduction of mortality has been discussed more controversial [19-24]. None of the trials suggesting a benefit in primary prevention actually achieved mean LDL-concentrations of less than 1.8 mmol/l. In one large metaanalysis subgroup analysis [25] showed a decreasing risk for cardiovascular events even below a LDL concentration of 1.8 mmol/l. So, the question arises where the optimal threshold for LDL concentration is. It must be acknowledged that lower LDL concentrations were usually achieved with a higher statin dose but also at the expense of a higher rate of stain related adverse effects. On the other hand, pleiotropic effects of statins potentially contribute to the reduced cardiovascular risk independently of the achieved LDL-concentrations. In the light of these uncertainties, the current guideline in the treatment of blood cholesterol to

reduce atherosclerotic cardiovascular risk in adults released by the American Heart Association even refrains from making recommendations for specific LDL target values for primary or secondary prevention [26].

Guidelines are based on the best available evidence and expert opinion. The underlying trials often concentrate only on one or a few parameters due to feasibility and study design. This often does not take in account the complex combinations of underlying disease in real life with multiple parameters affecting each other. As a result evidence on treating patients with multiple risk factors and multimorbid conditions is scarce [7].

The ESC/EASD guideline 2007 tended to treat each cardiovascular risk factor separately and primarily focused on specific risk groups, not considering other important factors as age and sex. Additive effects of controlling different risk factors at the same time, as shown in UKPDS [14] and STENO-2 [12] and considering sex, age and life expectancy may be more important than pursuing sharp treatment thresholds.

Thus, the most recent recommendations for treating diabetes [2, 26, 27] are a welcome contribution to this discussion, since different goals for HbA1c are addressed to the specific needs of different age groups, taking in account even individual needs and preferences. When measuring the outcomes of the patients in our study against the latest, more moderate target values, the evidence-performance gap decreased, especially regarding glycemic control and BP. Regarding LDL, the evidence-performance gap is actually not measurable anymore, because target levels are under discussion or even dropped. This finding substantiates the hypothesis that GPs in our study already adapted the guidelines to the needs of their patients before the guidelines have been officially revised.

To conclude, our study population is well treated regarding HbA1c, BP and LDL-concentrations compared to current evidence. Nevertheless, there is still room for improvement left, especially in regard to medication regimen.

5.3 Differences in medication use

Medication use among patients in our study differed in many cases from the medication prescribed in the other trials and guideline recommendations. Despite most of our patients being overweight, only little more than half were prescribed metformin, while in ADVANCE metformin was used in considerably more patients at baseline. Similarly, only approximately one third of the patients in our study received ACE inhibitors to lower blood pressure, although prevalence of hypertension was higher.

Similarly, statins were only used in less than half of our patients. Roughly a third of patients with a LDL-concentration above the treatment goal of less than 1.8 mmol/l were taking a statin. Interestingly in the ACCORD-trial, although four fifth of the study population was reported to take a statin at the end of follow up, the mean LDL-concentration was still clearly higher than the recommended threshold value by guidelines.

According to guidelines we would have expected a much higher proportion of patients among our study population receiving the above mentioned medication. Reasons for this gap can only be assumed. Non-adherence of patients may play a role in not reaching treatment goals. It may be due to the fact that the effect of these medications can only be visualized partially (for example by laboratory data) while perception of long term effects on risk reduction in the individual patient remain vague. This may attenuate awareness of the importance of prescribing these medications by the treating physicians. Also fear of polypharmacy and side effects may hinder physicians and patients in the use of multiple substances. Concerns of the treating physician in doing more harm than good by administering the treatment regimen as proposed by the guidelines as well as patient concerns must be taken into account.

5.4 Strength and limitations

The strength of our study is certainly the use of clinical real life data from patients with T2DM in Swiss primary care, including not only data on glycemic control but also on other cardiovascular risk factors. So far, similar data on Swiss patients with T2DM were either retrieved from secondary care or focused on different hypotheses.

For instance, Burgmann et al. have recently examined the metabolic control of Swiss patients with T2DM in light of international and national recommendations and concluded that metabolic control in these patients was less than optimal given a mean HbA1c of 7.7%, a hypertension rate of 80%, a mean LDL level of 2.6 mmol/l [28]. However, the study was a retrospective medical chart analysis of patients with T2DM admitted to a general internal medicine clinic. It is questionable if these data are qualified to represent Swiss primary care in general and not only a proportion of more urgent and severe cases that needed hospitalization.

In contrast, Gerber et al. have gathered data from primary care by conducting a national cross-sectional survey among 134 physicians and their patients in all four cultural regions of Switzerland [29]. The results point in the same direction as our results, demonstrating a bigger or smaller evidence-performance depending on the guideline used as

the state of the art (mean HbA1c 7.03±1.24%, mean systolic BP 138.5±16.6 mmHg, mean diastolic BP 81.4±10.3 mmHg, mean LDL 2.8 mmol/l, mean BMI 29.8). However it is to note, that the survey was primarily designed to detect local differences in the quality of diabetes care and to evaluate the role of different cultural backgrounds as predictor for the use and outcome of hyperglycemic medical therapy. In our study, we primarily aimed to assess the potential evidence-performance gap. Data were directly entered to the clinical information system by physicians during patients' consultations and reflect clinical routine data from primary care. To our knowledge, it is the first time that such data have been available for analysis in Switzerland.

It must be mentioned, however, that the lack of follow up in our study makes it impossible to compare glycemic and cardiovascular risk control as well as morbidity or mortality over time. Therefore, our results are limited to a cross-sectional view. It would be interesting to examine to what extent the recent publication of more moderate guidelines would influence the outcomes of primary care patients.

It should be acknowledged that data acquisition was not standardized throughout our study practices apart from the structure inherent in the electronic clinical information system used to record the consultations. On the one hand, this could be considered to be a limitation; on the other hand, it is to note that we aimed to obtain real life data. Determining standards for a routine consultation of patients with T2DM would have influenced the usual patterns of physicians' care and consequently unfold various effects on the physician-patient relation with unknown impact on patients' compliance and – at last – outcomes. Thus, our results should be interpreted as results of unregulated diabetes care in a primary setting where the responsibility for care management rests primarily with the physician. As such they might be representative for comparable health care systems.

6. Conclusion

We conclude that patients with T2DM in Swiss primary care are comparable to patient populations of large landmark studies that highlighted the necessity of individual treatment plans and indicated that very strict treatment goals are of no additional benefit. As a consequence, most patients in Swiss primary care would not benefit from a treatment intensification regarding target values of HbA1c, BP and cholesterol. Apparently, current guidelines are more applicable to this patient population than earlier versions were, but an evidence-performance gap rests regarding the choice of first line medication.

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Baseline Characteristics	Our study	UKPDS 1998	ACCORD 2008	ADVANCE 2008	STENO-2 1999	VADT 2009	ESC/EASD guideline 2007
Number of patients (n)	541 (32% women)	3867 (39% women)	10251 (39% women)	11140 (42% women)	160 (26% women)	1791	
Age (years)	68 ± 12	53 ± 9	62 ± 7	66 ± 6	55 ± 7	60 ± 9	
Duration of type 2 diabetes (years)	10.3 ± 7.8	<1 year	10 ± n.a.	8 ± 6	6	11.5 ± 8	
HbA1c (median %)	7.3 ± 1.2	7.1 ± 1.5	8.3 ± 1.1	7.2 ± 1.6	8.8 ± 1.6	9.4 ± 2.0	<6.5–7.0
Systolic blood pressure (mmHg)	135 ± 16	135 ± 20	136 ± 17	145 ± 22	149	132 ± 17	< 130
Diastolic blood pressure (mmHg)	78 ± 10	82 ± 10	75	81 ± 11	86	76 ± 10	< 80
LDL-level (mmol/l)	2.6 ± 1.0	3.5 ± 1.1	2.7 ± 0.9	3.1 ± 1.0	3.4	2.8 ± 0.8	< 1.8
Arterial Hypertension (prevalence %)	73%	n.a.		n.a.		n.a.	
BMI (kg/m ²)	29 ± 5	28 ± 5	32 ± 6	28 ± 5	31	31 ± 4	< 25
Obesity (prevalence %)	42%	n.a.		n.a.		n.a.	
Coronary heart disease (prevalence %)	13%	n.a.	35%	32%	37.5%	40%	
Current smoker (prevalence %)	7%	30%	14%	14%	38 %	17 %	
Multimorbidity [T2DM + at least 1 chronic condition] (prevalence %)	81%	n.a.	n.a.	n.a.	n.a.	n.a.	
Number of CVRF	1 to 4		at least 2	at least 1	at least 1	at least 1	
Target level of HbA1c in % in the intervention group			< 6.0	≤ 6.5	≤ 6.5	< 6.0	

Table 1. Patient characteristics according to study population and ESC/EASD guideline 2007. Data are presented as mean values ± standard deviation if not otherwise declared (n.a.=not available).

Medication	Our study	UKPDS 1998	ACCORD 2008	ADVANCE 2008	STENO-2 1999	VADT 2009
Metformin	58.6	n.a.		71.4	16.0	
Glitazone	1.5	n.a.		3.7	0	
Sulfonylurea	26.4	n.a.		63.5	54.5	
Glinide	1.9	n.a.		1.7	n.a.	
Insulin	16.1	n.a.	35.0	11.5	10.0	52.0
ACE-I	39.4	n.a.	52.9	n.a.	19.5	
AT II-Antagonist	14.8	n.a.		n.a.		
Calcium-Antagonists	18.3	n.a.		n.a.	10.0	
Diureticum	30.1	14.0		n.a.	24.5	
BB	24.8	n.a.	29.2	n.a.	5.5	
Aspirin	41.4	n.a.		44	14.0	
Marcoumar	4.4	n.a.		n.a.	n.a.	
Statin	41.6	n.a.	59.3	28.3	1.5	
Any antihypertensive drug	62.1	12.0	85.4	75.1	41.0	
Any lipid lowering drug	41.6	0.3		36.7		

Table 2. Medical treatment according to study population. Data are presented as % if not otherwise declared (n.a.=not available).