Non-interventional Study Report

Evaluation of treatment patterns for hypertensive diabetics to meet blood-pressure and glucose targets

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List of Abbreviations

ADA	American Diabetes Association
AE	Adverse Event
ARB	Angiotensin Receptor Blocker
BMI	Body Mass Index
BP	Blood Pressure
CRF	Case Report/Record Form
CRO	Contract Research Organization
CVD	Cardiovascular Disease
DBP	Diastolic Blood Pressure
DS&E	Drug Safety and Epidemiology
eCRF	electronic Case Report/Record Form
ENCePP	European Network of Centres for Pharmacoepidemiology and Pharmacovigilance
FBG	Fasting Blood Glucose
FPFV	First Patient First Visit
FPLV	First Patient Last Visit
FU	Follow-up
GPP	Good Pharmacoepidemiology Practices
HbA1c	Glycated Hemoglobin A1c
ICH	International Conference on Harmonization
IEC	Independent Ethics Committee
IRB	Institutional Review Board
ISPE	International Society for Pharmacoepidemiology
LPFV	Last Patient First Visit
LPLV	Last Patient Last Visit
MedDRA	Medical Dictionary for Regulatory Activities
NIS	Non-interventional Study
OAD	Oral Antidiabetics
PI	Principal Investigator
PRO	Patient Reported Outcome
QoL	Quality of Life
SAE	Serious Adverse Event

SBP	Systolic Blood Pressure
SOP	Standard Operating Procedure
SPC	Summary of Product Characteristics
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology
T2DM	Type 2 Diabetes Mellitus
WHO	World Health Organization

1 Synopsis

Title	DIALOGUE: Evaluation of treatment patterns for hypertensive diabetics to meet blood-pressure and glucose targets
Keywords	German, multi-center, prospective non-interventional registry
Rationale and background	Type 2 diabetes mellitus (T2DM) is considered a major epidemic worldwide. Diabetic patients are at an increased risk for disease and treatment related complications and frequently show distinct comorbidities such as obesity, dyslipidemia and in approximately 90 % hypertension (Bramlage et al., 2010). Especially hypertension is a major risk factor for cardiovascular morbidity and mortality in patients with diabetes. Patients with type 2 diabetes have a two- to fourfold greater risk of cardiovascular death than those without diabetes (Haffner et al., 1998) and the combination of both hypertension and diabetes even doubles the risk of stroke, death from cardiovascular causes, and all-cause mortality when compared with that of non-diabetic hypertensive patients. In addition, hypertension contributes to the progression of diabetic nephropathy, retinopathy, left ventricular hypertrophy, and diastolic heart failure.
Research question and objectives	The purpose of the present study was to evaluate various treatment patterns of antidiabetic (including incretin-based and exclusively non-incretin-based therapies) and anti-hypertensive treatments (including RAAS-inhibitors and exclusively non-RAAS-inhibitors) as well as their combinations, patient reported outcomes and treatment success in hypertensive type 2 diabetes mellitus patients in a prospective, observational, national, multicenter registry 24 months after occurrence of a change in their antidiabetic treatment with interim analyses performed at 6 months and 12 months in primary care and diabetology centers in Germany.
Study design	This non-interventional study was designed as a prospective multi-center registry encompassing 10,000 patients with diabetes mellitus and hypertension to evaluate medical care in a real-life setting in Germany. The enrolment period started in July 2012 (FPFV: 12 July 2012). The registry did not require or recommend or discourage any treatments just for the sake of inclusion into the registry that was beyond standard routine care for the patient. In that sense, it was strictly neutral and served the sole purpose of documentation of the current treatment practice in diabetics with hypertension treatment in clinical practice in Germany.
Setting	Centers were selected to be representative for the ambulatory treatment of patients with diabetes and/or hypertension in Germany. For this purpose, a representative cross-section of different centers including diabetologists and primary care physicians was selected. It was planned to identify up to 700 study sites. Data were recorded at baseline and prospectively documented by the participating sites during follow-up visits at 6, 12 and 24 months. Patient recruitment started on 12th June 2012 and ended on 28th January 2014. Recruitment of patients was planned to be concluded by March 2013, but had to be extended to January 2014 to obtain a sufficient amount of patients, i.e. converging to the planned sample size of 10,000 patients. On 1st July 2014, the antidiabetics Galvus®/Eucreas® (Vildagliptin/Vildagliptin plus Metformin) were withdrawn from the market, thus, the registry, i.e. documentation of follow-up visits, was prematurely concluded on 30th December 2014; database was closed on 2nd February 2015 for sites and on 11th May 2015 for reconciliation of safety data.

Subjects and study size, including dropouts	Patients were consecutively enrolled according to a pre-specified ratio based on their treatment, which was not predetermined by the study protocol but based on the physician's decision. "Incretin-based treatment" is defined as either a DPP-4 inhibitor or a GLP-1 analogue. "Non-incretin-based treatment" is defined as any of the following: metformin, sulfonylureas, acarbose, insulin, alpha-glucosidase inhibitors, and/or SGLT2-inhibitors. As the clinical profile of vildagliptin appears to differ from that of other DPP-4 inhibitors, the "incretin-based treatment" group are split into those with or without vildagliptin. To attain an approximation of representative coverage of 0.2 – 0.25 % of all T2DM patients in Germany (based on data given by Classen et al., 2009 "Innere Medizin", Urban&Fischer), a sample size of 10,000 was planned to be evaluated within this observational study. This sample size ensures strong and robust data even in various sub-populations that are of interest in T2DM defined in the secondary objectives (e.g. elderly, patients with renal impairment, women, insulin add-on during the course of study etc.). As the focus of this registry lay on diabetes, strata based on antidiabetic treatment were pre-defined. Therefore, the overall registry population of 10,000 patients comorbid with diabetes and hypertension was planned to be divided into 2 treatment strata (incretin-based treatment: n = 6,000; non-incretin-based: n = 4,000). The enrolment ratio of incretin-based treatment stratum was planned to be 2:1 for vildagliptin (n = 4,000) and other incretin-based treatments (n = 2,000). Ultimately, n=8,568 hypertensive T2DM patients were enrolled at baseline (incretin-based treatment: n= 5577 [65.1%]; non-incretin-based treatment: n= 2991 [34.9%]). Among patients with incretin-based therapy, n= 3487 (62.5%) patients were treated with vildagliptin. Follow-up at 6 months after baseline was documented for n= 7,355 patients (85.5%), at 12 months for n= 6691 patients (78.1%), and at 24 months for n= 4130 patients (48.2%).
Variables and data sources	The following parameters were documented at baseline and at 6M-/12M-/24M-Follow-up (overview): • Sociodemographic characteristics • Physical examination • Cardiovascular concomitant diseases • Diabetes associated diseases • Available laboratory values • Antidiabetic medication • Additional current medication • Hypoglycemic events • QoL (EuroQoL-5D) • Patient reported outcome
Results	Overall, 8,568 hypertensive T2DM patients from 511 active sites were enrolled at baseline. Among those 2,991 patients (34.9%) were initially treated with non-incretin-based medication and 5,577 patients with incretin-based medication. Among patients with incretin-based therapy, 3,487 (62.5%) patients were treated with vildagliptin and 2,090 (37.5%) with other incretin-based medication. Patients were followed-up at 6, 12, and 24 months after baseline visit. Numbers of documented follow-up visits at 24 months were particularly low (only about 50% of all enrolled patients had documented follow-up visits at 24 months), since not all patients had a 24-month follow-up visit (due to the fact that on 1st July 2014, the antidiabetics Galvus®/Eucreas® were withdrawn from the market, and thus, the registry and the documentation of follow-up visits was prematurely concluded in December 2014).

	For the evaluation of individualized treatment targets and their achievement patients were categorized into three groups based on treatment goals regarding (1) initial HbA1c treatment goals (≤ 6.5% [strict] / >6.5 – 7.0% [medium] / >7.0 – ≤ 7.5% [loose]) and on (2) initial SBP treatment goals (≤ 130 mmHg [strict] / >130 – 135 mmHg [medium] / >135 – - ≤ 140 mmHg [loose]). Multivariate analyses regarding factors contributing to the assignment of patients into the loose target groups for both HbA1c and SBP revealed that loose HbA1c targets were weakly correlated with age, gender, fasting blood glucose, SBP, heart failure and peripheral arterial disease with the HbA1c value at baseline as the strongest predictor. Similarly, loose SBP targets were weakly correlated with age, fasting blood glucose, heart failure, peripheral arterial disease, and neuropathy with the SBP value at baseline as the strongest predictor. Analyses of the relationship between patients with distinct HbA1c and SBP treatment goals showed that about 70% of patients with strict HbA1c treatment targets also had strict SBP treatment goals. The same could be observed for cross comparison of the medium and loose treatment groups (about 52% and 61% of patients in the respective HbA1c target groups coincided with the corresponding SBP target groups). Target achievement rates were calculated for 6-, 12-, and 24-month follow-ups. Regarding the HbA1c treatment targets, at least about half of the patients met their pre-defined treatment targets (strict target: 45.8% at 6M-FU, 46.2% at 12M-FU, 46% at 24M-FU; medium target: 51.4% at 6M-FU, 56.8% at 12M-FU, 61.5% at 24M-FU; loose target: 53.3% at 6M-FU, 59.4% at 12M-FU, 64.5% at 24M-FU). Regarding the SBP treatment targets, more than 50% of the patients met their pre-defined treatment targets (strict target: 51.4% at 6M-FU, 50.8% at 12M-FU, 50.3% at 24M-FU; medium target: 54.5% at 6M-FU, 56.4% at 12M-FU, 60.6% at 24M-FU; loose target: 65.0% at 6M-FU, 67.3% at 12M-FU, 72.4% at 24M-FU).
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General Information

This Non-interventional Study Report has been written based on the following documents for the DIALOGUE registry:

- Observational Plan (Version02, dated 06-OCT-2014)
- Statistical Analysis Plan (Version DRAFT1.1, dated 24-NOV-2012)

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4 Milestones

Table 4-1. *Study milestones*

Milestone	Planned date	Actual date
Start of data collection	JUN 2012	12 JUL 2012
End of data collection	JUN 2015	31 JAN 2015
First Patient First Visit – FPFV	JUN 2012	12 JUL 2012
Last Patient First Visit – LPFV	MAR 2013	28 JAN 2014
First Patient Last Visit – FPLV (24M-FU)	JUN 2014	04 JUN 2014
Last Patient Last Visit – LPLV (24M-FU)	MAR 2015	30 JAN 2015
Database closure (for participating sites)	--	02 FEB 2015
Database closure (for reconciliation)	--	11 MAY 2015
Final report of study results	APR 2016	15 DEC 2015
Protocol approval by IRB/IEC	Q2 2012	9 JUL 2012

5 Rationale and Background

Type 2 diabetes mellitus (T2DM) is considered to be a major epidemic worldwide. Diabetic patients are at an increased risk for disease and treatment related complications and frequently show distinct comorbidities such as obesity, dyslipidemia and in approximately 90 % hypertension (Bramlage et al., 2010). Especially hypertension is a major risk factor for cardiovascular morbidity and mortality in patients with diabetes. Patients with type 2 diabetes have a two- to fourfold greater risk of cardiovascular death than those without diabetes (Haffner et al., 1998) and the combination of both hypertension and diabetes even doubles the risk of stroke, death from cardiovascular causes, and all-cause mortality when compared with that of non-diabetic hypertensive patients. In addition, hypertension contributes to the progression of diabetic nephropathy, retinopathy, left ventricular hypertrophy, and diastolic heart failure.

An observational analysis of the United Kingdom Prospective Diabetes Study (UKPDS) data showed that the risk of both - macrovascular and microvascular - complications of type 2 diabetes was strongly associated with mean systolic blood pressure and that BP lowering by

10 mmHg was associated with a 15% reduction in the risk of death related to diabetes (Adler et al., 2000).

Thus, in diabetic patients with hypertension, both, appropriate blood pressure control as well as glucose control is important. Current guidelines recommend a multifactorial approach with simultaneous targeting of blood pressure and glucose levels in individuals with type 2 diabetes. Unfortunately, less than one third of the hypertensive diabetics meet their current blood pressure target of 130/80 mmHg and less than half of them the HbA1c target of ≤ 6.5%. Therefore, an adequate combined antidiabetic and anti-hypertensive treatment is needed to provide sufficient control in hypertensive diabetic patients.

During the past years, new medications and fixed dose combinations have been developed for both indications, i.e. diabetes mellitus type 2 and hypertension. To treat the latter, RAAS-inhibitors as well as non-RAAS inhibitors nowadays exist and are available in several fixed dose combinations with calcium channel blockers like amlodipine and/or diuretics like hydrochlorothiazide. For aiming glycemic control incretin-based treatments like DPP-4 inhibitors (vildagliptin, sitagliptin, saxagliptin) revealed a potent strategy and are increasingly used in fixed dose combinations (e.g. with metformin) as well.

Interestingly, the use of fixed dose combinations has shown to significantly improve compliance by reducing pill burden (Bangalore et al., 2007), which results in higher rates of reaching target values and less hospitalization rates.

As drugs belonging to the class of DPP-4 inhibitors (Gliptins) have different properties, e.g. pharmacokinetics, they influence the glycemic profile in T2DM – patients in different ways. This has been shown in a study published by Marfella (2010), where sitagliptin and vildagliptin were compared as add-on therapies to metformin regarding effectiveness in improving the 24 h-blood glucose profile (measured as MAGE). The improvements of glucose fluctuations over a day (MAGE) were more pronounced in the vildagliptin than in the sitagliptin group. Since glucose variations over time, linked to daily fluctuations of glucose, are associated with an activation of oxidative stress, the main mechanisms that lead to chronic diabetic complications (Monnier et al., 2006), these data suggest that a therapy should target not only reducing HbA1c but also flattening acute glucose fluctuations over time to positively influence the outcome of type 2 diabetic patients. As the study of Marfella only evaluated 38 patients during a short period of time (12 weeks) it is of further interest of this observational study to gain more data about this effect and the impact in a real-life setting. As vildagliptin seems to have the strongest effect on flattening acute glucose fluctuations among DPP-4 inhibitors this substance has been chosen for evaluating this effect. To ensure a potent sample size for gaining sufficient data on this question a stratification is planned within the group of incretin-based-therapies of 2:1 – vildagliptin : other incretin based therapies.

Nowadays, treatment suggestions and treatment efficacy are primarily based on guidelines justified on evidence from randomized controlled trials. However, these trials reflect only selected patients. Patients seen in daily practice normally are older and suffer from more comorbid diseases as compared to those in clinical trials. Little is known about the current patient characteristics, treatments and outcome of diabetics with hypertension in clinical practice, especially with respect to the use of newly developed and approved anti-hypertensive and antidiabetic compounds.

Additionally, it is quite unclear if and how the different combinations of treatments are able to meet the remaining unmet medical need and how several distinct combinations of antidiabetic and anti-hypertensive medications together contribute to aim for and preserve target blood-glucose- and blood-pressure-values individually chosen in accordance with each patients constitution.

The present registry was designed to evaluate various treatment patterns and combinations (antidiabetic and anti-hypertensive treatments), as well as their success in aiming for blood-pressure- and glycemic control in hypertensive type 2 diabetes mellitus patients in Germany after 24 months with interim analyses performed at 6 and 12 months and optional follow-ups after 36 and 48 months.

6 Research Question and Objectives

The purpose of the present study was to evaluate various treatment patterns of antidiabetic (including incretin-based and exclusively non-incretin-based therapies) and anti-hypertensive treatments (including RAAS-inhibitors and exclusively non-RAAS-inhibitors) as well as their combinations, patient reported outcomes and treatment success in hypertensive type 2 diabetes mellitus patients in a prospective, observational, national, multicenter registry 24 months after occurrence of a change in their antidiabetic treatment with interim analyses performed at 6 months and 12 months as well as an optional follow-up at 36 months and 48 months in primary care and diabetology centers in Germany.

6.1 Primary Objectives

To determine individual treatment success of different antidiabetic (incretin-based and non-incretin-based) *and* antihypertensive (RAAS-inhibitor and non-RAAS-inhibitors) medications and their combinations by defining the number of T2DM hypertensive patients who reach their blood glucose target values and blood pressure targets as pre-defined by treating physician based on current guidelines given by the DDG (Matthaei et al., 2011) and the ESH (Mancia et al., 2009) and remain controlled over the observational period of 24 months (interim analyses performed at 6 months and 12 months, optional 36- and 48-months follow-up).

6.2 Secondary Objectives

- To assess the proportion of patients reaching their blood glucose target values without any of the following adverse effects: peripheral edema *or* proven hypoglycemic event *or* discontinuation due to gastrointestinal event *or* significant weight gain (>5 %)
- To describe patient characteristics in patients with diabetes mellitus and hypertension in clinical practice in the overall registry population
- To document antidiabetic and anti-hypertensive therapy and its success in diverse subject populations, which have to be pre-specified by the scientific committee (e.g. females versus males, age </>75y, patients on insulin versus patients not on insulin, etc.)

- To verify the applicability of and the adherence to the current guidelines for the treatment of diabetes and hypertension in clinical practice
- To document drug utilization patterns of medication used for the treatment of diabetes as well as hypertension in clinical practice
- To evaluate adverse cardiovascular events, and diabetes related micro- and macrovascular events
- To evaluate the glycemic profile
- To evaluate the blood pressure profile
- To evaluate comorbid disease conditions
- To evaluate the change of the BMI over the course of the study
- To evaluate the proportion of patients with hypoglycemic events
- To evaluate cardiovascular risk by using validated cardiovascular risk scores such as the EURO Score
- To evaluate the subjective health status (EQ-5D)
- To determine costs associated with the treatment and disease-related complications
- To document treatment persistence over time, change in treatments / dosing during a follow-up of years (optional up to 4 years of follow-up)
- To document patient reported outcome (PRO)

7 Amendments and Updates to the Protocol

There were no amendments to the study protocol that required re-approval of the IRB/IEC.

8 Research Methods

8.1 Study Design

This non-interventional study was designed as a prospective multi-center registry (non-interventional, observational study) encompassing 10,000 patients with diabetes mellitus and hypertension to evaluate medical care in a real-life setting in Germany. The enrolment period started in July 2012 (FPFV: 12 July 2012) with a follow-up of up to 24 months (i.e., follow-up at 6, 12, and 24 months).

The registry did not require or recommend or discourage any treatments just for the sake of inclusion into the registry that was beyond standard routine care for the patient. In that sense, it was strictly neutral and served the sole purpose of documentation of the current treatment practice in diabetics with hypertension treatment in clinical practice in Germany.

To attain an approximation of representative coverage of 0,2 – 0,25 % of all T2DM patients in Germany (based on data given by Classen et al., 2009 “Innere Medizin”, Urban&Fischer publishing house), a sample size of 10,000 was planned to be evaluated within this observational study. This sample size ensures strong and robust data even in various sub-

populations that are of interest in T2DM defined in the secondary objectives (e.g. elderly, patients with renal impairment, women, insulin add-on during the course of study etc.).

As the focus of this registry lay on diabetes, strata based on antidiabetic treatment were pre-defined (see Figure 8-1). Therefore, the overall registry population of 10,000 patients comorbid with diabetes and hypertension was planned to be divided into 2 treatment strata (incretin-based treatment: n = 6,000; non-incretin-based: n = 4,000). The enrolment ratio of incretin-based treatment stratum was planned to be 2 : 1 for vildagliptin (n = 4,000) and other incretin-based treatments (n = 2,000).

Patients were eligible for inclusion, if treated with oral mono or dual combination therapy and were distributed into the following groups: (1) Incretin-based treatments such as DPP-4 inhibitors, GLP-1 analogues. (2) Non-incretin-based therapies such as Metformin, Sulfonylureas, Acarbose, Insulin, alpha-Glucosidase Inhibitors, SGLT2-Inhibitors.

This registry was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and adhere to the principles of Good Epidemiology Practice (GEP), and applicable regulatory requirements. The protocol of this registry was approved by the ethics committee of the Ruhr University Bochum, Germany. Patients that were being enrolled into this registry provided written informed consent. DIALOGUE has further been registered in the database of the Verband forschender Arzneimittelhersteller (VFA).

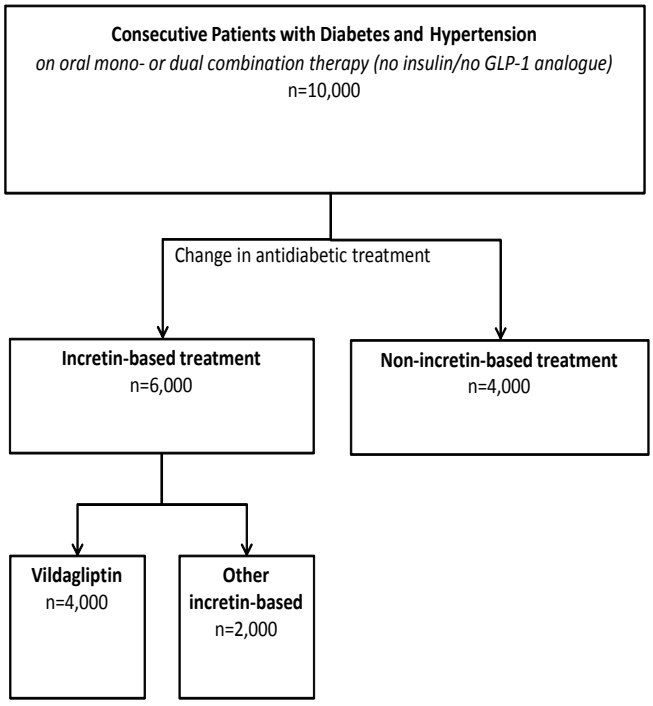

Figure 8-1. *Planned sample size and segmentation into strata of different antidiabetic-treatments.*

8.2 Setting

Selection of centers

Centers were selected to be representative for the ambulatory treatment of patients with diabetes and/or hypertension in Germany. For this purpose, a representative cross-section of different centers including diabetologists and primary care physicians was selected. It was planned to identify up to 700 study sites.

All participating sites were paid investigator fees for complete datasets per visit, as follows:

Baseline visit	€ 70,00
6M-FU	€ 40,00
12M-FU	€ 60,00
24M-FU	€ 70,00

Study visits

Data were recorded at baseline and prospectively documented by the participating sites during follow-up visits at 6, 12 and 24 months. Patient recruitment started on 12th June 2012 and ended on 28th January 2014. Recruitment of patients was planned to be concluded by March 2013, but had to be extended to January 2014 to obtain a sufficient amount of patients, i.e. converging to the planned sample size of 10,000 patients. On 1st July 2014, the antidiabetics Galvus®/Eucreas® (Vildagliptin/Vildagliptin plus Metformin) were withdrawn from the market, thus, the registry (i.e. documentation of follow-up visits) was prematurely concluded in December 2014; database was closed on 2nd February 2015 for sites and on 11th May 2015 for reconciliation of adverse events.

8.3 Subjects

Patients were consecutively enrolled according to a pre-specified ratio based on their treatment, which was not predetermined by the study protocol but based on the physician's decision. "Incretin-based treatment" is defined as either a DPP-4 inhibitor or a GLP-1 analogue. "Non-incretin-based treatment" is defined as any of the following: metformin, sulfonylureas, acarbose, insulin, alpha-glucosidase inhibitors, and/or SGLT2-inhibitors. As the clinical profile of vildagliptin appears to differ from that of other DPP-4 inhibitors, the "incretin-based treatment" group are split into those with or without vildagliptin (see Figure 8-1).

Physicians were asked to collect prospective data as outlined in the inclusion criteria. The physician was completely free in his choice regarding antidiabetic and antihypertensive treatment; enrolment, however, was limited according to the pre-specified ratio. The electronic documentation was provided with a specialized tool displaying the current status of enrolment ratio on site level. This allows for documenting patients across different time periods within different strata.

Inclusion criteria

Patients were eligible for inclusion in this registry if the following criteria applied:

- Age: ≥18 years
- Diagnosed type- 2 diabetes mellitus and manifested hypertension (Comorbidity)
- Antidiabetic therapy presently on oral mono- or dual combination therapy
- Treating physician considers blood glucose lowering medication to be not adequate and/or not safe/tolerable
- The physician adds another oral drug / switches drug treatment to achieve glycemic control
- Written informed consent for participation obtained from the subject.

Exclusion Criteria

Patients were not eligible for inclusion in this registry if any of the following criteria applied:

- Current Participation in any randomized controlled trial.
- Patients not under regular supervision of the treating physician for the duration of the study
- Use of GLP-1-analogues or insulin before enrolment
- Patients treated with aliskiren in a dual renin angiotensin aldosterone (RAAS) blockade
- Pregnancy
- Diabetes secondary to malnutrition, infection or surgery
- Maturity onset diabetes of the young
- Known cancer

8.4 Variables

Table 8-1. *Overview of documented parameters*

Visit	Baseline	6M-FU	12M-FU	24M-FU
Sociodemographics[1]	X			
Physical examination[2]	X			
Cardiovascular concomitant diseases[3]	X	X	X	X
Diabetes associated diseases[4]	X	X	X	X
Available laboratory values[5]	X	X	X	X
Antidiabetic medication[6]	X	X	X	X
Additional current medication[7]	X	X	X	X
Hypoglycemic events[8]	X	X	X	X
QoL (EuroQoL-5D)	X	X	X	X
Patient reported outcome	X	X	X	X

Legend: 1) age, gender, insurance status, DMP participation, education, employment status, care level 2) weight, height, waist circumference, smoking, alcohol consumption, physical activity 3) coronary heart disease, previous myocardial infarction, previous PCI, previous CABG, previous stroke, heart failure (NYHA) peripheral artery occlusive disease 4) dyslipidemia, amputation, autonomous neuropathy, non- proliferative/proliferative retinopathy, diabetic macular edema, blindness, dialysis other 5) less than six weeks old: lipid values (fasting total cholesterol, fasting LDL, fasting HDL, triglycerides), fasting and post-prandial blood glucose, HbA1c, renal values (serum creatinine, microalbustix albumin, microalbustix creatinine), liver parameters. 6) metformin, sulfonylureas, glucosidase inhibitors, glinides, glitazones, DPP-4 inhibitors) 7) ACE inhibitors, ARBs, renin inhibitors, beta blockers, calcium channel blockers, diuretics, other) 8) 12 months before baseline visit and since baseline or last FU, respectively.

The following parameters were collected <u>once for all participating sites</u>:

- Personal information on participating physician (name, title, address, date of birth, professional education, further education and specific medical qualification, type of medical practice, account details for reimbursement, preferred measurement units at the site)

The following parameters were collected <u>only at baseline visit</u>:

- Sociodemographics (age, gender, insurance status, disease management participation, education as assessed by number of years at school, employment/retirement status, care levels), weight, height, waist circumference, smoking, frequency of alcohol consumption, physical activity

The following parameters were collected <u>at baseline visit and each follow up visit</u>:

- Cardiovascular concomitant diseases (coronary heart disease, previous myocardial infarction, previous PCI, previous bypass surgery, previous stroke, heart failure with NYHA class, peripheral artery occlusive disease), diabetes associated diseases (dyslipidemia, amputation, autonomous neuropathy, non-proliferative diabetic retinopathy, proliferative diabetic retinopathy, diabetic macular edema, blindness, dialyses, other).

- Available laboratory parameters (less than 6 weeks old): Lipid values (fasting total cholesterol, fasting LDL cholesterol, fasting HDL cholesterol, triglycerides), fasting blood glucose, post-prandial blood glucose, HbA1, renal values (serum creatinine, microalbustix albumin, microalbustix creatinine), liver values
- Anti-diabetic medication (before and at the time of inclusion): metformin, sulfonylurea, glucosidase inhibitors, glinides, glitazones, DPP-4-inhibitor
- Current antihypertensive medication (ACE inhibitors, Angiotensin receptor blockers (ARB), renin inhibitors, beta-blockers, calcium channel blocker, diuretic, other)
- QoL (EuroQoL-5D)

The following parameters were collected for each adverse event:

- Patient's personal information (date of AE/SAE documentation, ID, date of birth, sex, ethnic group, weight, height)
- Information on adverse event (severity, start, end, outcome, hospitalization, date of hospital admission, date of dismissal, autopsy)
- Medication (causality for AE/SAE, pharmaceutical product, medical indication, start of medication, dose, treatments, end of medication)
- Previous disease (start, ongoing at time of AE/SAE, end of disease)
- Treatment because of AE/SAE (type of treatment, start, end, dose)
- Relevant data from laboratory tests and medical examination (date, type of measure, results, standard value)

8.5 Data Sources and Measurement

Patient information was collected directly at the participating sites: baseline data were documented in primary care and diabetes centers during the baseline visit. Follow-up visit information was documented at 6, 12, and 24 months after baseline. All study-relevant patient data was documented pseudonymously in the eCRF.

The patients had to complete the quality of life questionnaire (EuroQol 5D) handwritten; these data were captured in a separate database.

All data (except the QoL data) were collected via a remote, web-based data collection form using the software solution EBogen©, developed by the IHF Ludwigshafen, Germany.

Safety related measurements: The following parameters were collected for each adverse event (see section 8.4):

- Patient's personal information (date of AE/SAE documentation, ID, date of birth, sex, ethnic group, weight, height)
- Information on adverse event (severity, start, end, outcome, hospitalization, date of hospital admission, date of dismissal, autopsy)
- Medication (causality for AE/SAE, pharmaceutical product, medical indication, start of medication, dose, treatments, end of medication)

- Previous disease (start, ongoing at time of AE/SAE, end of disease)
- Treatment because of AE/SAE (type of treatment, start, end, dose)
- Relevant data from laboratory tests and medical examination (date, type of measure, results, standard value)

8.6 Bias

For efforts to assess and address potential sources of bias, refer to section 8.7 (justification of study size).

8.7 Study Size

To attain an approximation of representative coverage of 0.2 – 0.25 % of all T2DM patients in Germany (based on data given by Classen et al., 2009 "Innere Medizin", Urban&Fischer), a sample size of 10,000 was planned to be evaluated within this observational study. This sample size ensures strong and robust data even in various sub-populations that are of interest in T2DM defined in the secondary objectives (e.g. elderly, patients with renal impairment, women, insulin add-on during the course of study etc.).

As the focus of this registry lay on diabetes, strata based on antidiabetic treatment were pre-defined. Therefore, the overall registry population of 10,000 patients comorbid with diabetes and hypertension was planned to be divided into 2 treatment strata (incretin-based treatment: n = 6,000; non-incretin-based: n = 4,000). The enrolment ratio of incretin-based treatment stratum was planned to be 2 : 1 for vildagliptin (n = 4,000) and other incretin-based treatments (n = 2,000).

8.8 Data Transformation

The following variables were calculated from the collected (measured) data to perform the analyses mentioned in chapters below.

At baseline visit:

- Age, as the difference between date of enrollment and year of birth
- Time since manifestation of diabetes
- Duration of antidiabetic premedication before inclusion in Dialogue
- EURO score

At each visit:

- Values recorded in more than one SI unit (e.g. lab units) were converted into a single appropriate SI unit
- eGFR by MDRD formula
- Attainment of pre-defined target values for blood glucose and blood pressure
- Quality of life score

At each follow up visit:

- Time between follow up visit and baseline visit
- Changes (absolute and relative) of clinical parameters (blood pressure, heart rate, Weight, BMI, waist circumference) since baseline
- Changes (absolute and relative) of lab parameters since baseline, negative values represent a negative improvement from baseline, positive values will reflect a positive improvement from baseline
- Changes of medication (substance and daily dose)
- Time to events since baseline

8.9 Statistical Methods

8.9.1 Main summary measures

All items shown in the DIALOGUE registry Clinical Research Form (CRF) and all derived parameters are presented in a descriptive statistical report. The data evaluation was performed for the total population and the three treatments groups (1: Vildagliptin, 2: incretin-based treatment, 3: Non-incretin-based treatment) at baseline in comparison:

- Binary, categorical, and ordinal parameters are described by using absolute and percentage numbers within the various categories (including 'missing data' as valid category).
- Numerical data are described by using median, lower and upper quartile, number of missing data, minimum, and maximum.

8.9.2 Primary objectives

The primary endpoint of the DIALOGUE Registry was the individual treatment success of different anti-diabetic (incretin-based and non-incretin-based) and antihypertensive (RAAS-inhibitor and non-RAAS-inhibitors) medications and their combinations over the observational period of 24 months. Success was measured by defining the number of T2DM hypertensive patients who reached their blood glucose target values and blood pressure targets as pre-defined by treating physician based on current guidelines given by Position Statement of ADA and EASD (Inzucchi et al., 2012).

Therefore, treatment success is quantified by the numbers of patients in four groups with varying outcome: Patients, who have met both their predefined blood glucose and blood pressure target values, patients, who have reached one or the other target value and patients failing to meet any of target values.

The data evaluation was performed for the total population and the three treatments target groups

- Initial target HbA1c: ≤ 6.5% [strict] / >6.5 – 7.0% [medium] / >7.0 – ≤ 7.5% [loose]

- Initial target systolic BP: ≤ 130 mmHg [strict] / >130 – 135 mmHg [medium] / >135 – - ≤ 140 mmHg [loose])

at baseline in comparison.

For identifying independent associations between patient characteristics at baseline, medication and treatment success, logistic regression analyses were performed with the dependent binary variable success (yes/no). If no fixed parameter set was defined for the use as independent variables by the steering committee, all multivariable regression models were stepwise models. All parameters with a p-value < 0.1 (univariate comparison) were taken into consideration.

As mentioned above, for analyzing the glycemic profile, lipid profile, blood pressure profile and body weight during follow up, the relative and absolute change to baseline was calculated.

8.9.3 Laboratory data

Medians and quartiles or means and standard deviations are provided for baseline and at each follow-up visit for the following laboratory parameters as far as available:

- Fasting total cholesterol
- Fasting HDL- cholesterol
- Fasting LDL- cholesterol
- Fasting triglycerides
- fasting blood glucose
- Postprandial blood glucose
- HbA1c
- Hb
- Serum creatinine
- Microalbustix Albumin
- Microalbustix creatinine

Changes in laboratory data from baseline to follow-up visits were only provided for patients with both measurements.

8.9.4 Safety analyses

AE/SAE data and outcome data of the DIALOGUE registry

For all patients of the DIALOGUE registry, outcome data for specific events were captured in the eCRF by the treating physician (see section 8.4). Additionally, during the entire follow-up period AEs/SAEs of all DIALOGUE patients were documented independently by the treating physician. AE/SAE data and event data were analyzed and reported independently. An additional check was performed by Novartis for the events death, MI, PCI; stroke, CABG and hospitalization due to hypertension as follows:

– For each event in the outcome data of the DIALOGUE registry Novartis checked whether the corresponding event was documented in the AE/SAE database with respect to the presence of the event and number of events.

Stratification of AE/SAE data

AE/SAE data were stratified as follows:

Adverse Event (AE): any undesired event (serious + non-serious, suspected + non-suspected) with the following subcategories:

- **nsAE**: any non-serious adverse event (non-serious, suspected + unsuspected) with the following subcategories:
    - **nsADR**: non-serious adverse drug reaction; causality assessment: certain, probable/likely, possible, unassessable/unclassifiable, missing.
    - **nsAEnr**: non-serious adverse event not related; causality assessment: not related or unlikely.
- **SAE**: any serious adverse event (serious, suspected + unsuspected) with the following subcategories:
    - **SADR**: serious adverse drug reaction; causality assessment: certain, probable/likely, possible, unassessable/unclassifiable, missing.
    - **SAEnr**: serious adverse event not related; causality assessment: not related or unlikely.

Generation of line listings of AE/SAE data

The following line listings were generated:

- Line listing of non-serious adverse events (separately for nsADR and nsAEnr, including: site and patient ID/number, age, gender, medication taken [daily dose, treatment duration], event start date, event duration, event intensity, action taken, event outcome, causality assessment, event term verbatim, MedDRA Preferred Term, concomitant medication, medical history).
- Line listing of serious adverse events – excluding deaths (separately for SADR and SAEnr, including: site and patient ID/number, age, gender, medication taken [daily dose, treatment duration], event start date, event duration, event intensity, action taken, event outcome, causality assessment, event term verbatim, MedDRA Preferred Term, concomitant medication, medical history).
- Line listing of serious adverse events – including deaths (separately for SADR and SAEnr, including: site and patient ID/number, age, gender, medication taken [daily dose, treatment duration], event start date, event duration, event intensity, action taken, event outcome, causality assessment, event term verbatim, MedDRA Preferred Term, concomitant medication, medical history, date of death, cause of death).
- Line listing of pregnancies, including any adverse event and pregnancy outcome.

8.9.5 Statistical methods applied to the study

Continuous variables were summarized using standard statistics (i.e., mean, standard deviation, minimum, median, maximum, lower and upper quartile), whereas percentages were calculated for categorical data. There are no formal statistical test problems defined in DIALOGUE. Nevertheless, univariate comparisons between treatment groups were performed using Chi-Square, Kruskal-Wallis, or Log-rank test, as appropriate. Predictors for target group selection were identified through multivariate analysis. P-values ≤ 0.05 were considered to be significant. All statistical analyses were performed using SAS (release 9.3 or higher; Cary, NC, USA).

8.9.6 Missing data

Missing values for parameters were accepted for the statistical analyses and reported as missing values. If necessary for multivariable models, the principle of 'Last observation carried forward' was used especially for clinical parameters (blood pressure, heart rate, Weight, BMI, waist circumference) and lab parameters.

8.10 Quality control

All data (except the QoL data) were collected via a remote, web-based data collection form using the software solution EBogen©, developed by the IHF Ludwigshafen, Germany.

In the eCRF, each individual patient dataset was denoted by a univocal identification number, comprised of the site number, the consecutive patient number and the visit number (baseline or follow-up).

Data quality assurance included handling rules for missing or incomplete data, and range checks (i.e., age, date, etc.), along with data transformations (as agreed upon by all parties).

There are two strategies for data quality checks: validations that occur at the time of data entry (i.e., "front-end") and a second, more sophisticated quality control program that runs as a prelude to the creation of the analysis data set and on-site data monitoring.

Front-end data checks are advantageous because mistakes are caught and corrected at the time of entry – a system that is efficient for data collectors. Certain data elements can be required, while other variables may allow for missing values. Additionally, parameters were defined to allow entry of only those records that meet inclusion criteria.

Prior to the creation of the analytic dataset, more extensive quality control processes were performed. These checks, programmed in SAS, include parent–child edits, consistency edits, and data transformations that facilitate analyses.

Source documentation and data accuracy was verified during site visits in randomly selected ca. 2% of the sites. Overall, 13 sites (of 511 active sites) were monitored. It was specified to check a maximum of 10 patients per site. During on-site monitoring, the monitor verified informed consent documentation and performed source data verification against the patient's medical records (i.e. in-/exclusion criteria; event reporting; primary disease), fully respecting privacy and personal data of patients. Ultimately, apart from one participating site, all monitored sites were considered qualified for participating in a non-interventional study. Most

frequent findings were deficiencies in safety reporting, which is a typical finding in sites with only little experience in study participation. Data from one site had to be deleted completely from the study database, since several patients enrolled there had obviously not given written informed consent and the patients' medical records did not agree with data documented in the eCRF.

9 Results

In this section, the results of this registry are presented. The final study report is based on the final analysis of the data snapshot 8th June 2015. Due to the high amount of data, this report concentrates on the most important aspects that address the imminent research questions and objectives of the registry. Additional analyses are given in the appendices.

Section 9.1 of this report describes the patient flow in this registry (i.e. number of documented patients at baseline and follow-up visits). Section 9.2 describes the patient population based on the baseline data. Sections 9.3 and 9.4 specify the main outcome data regarding individualized therapy targets and individual treatment success as well as outcome data from follow-up. Section 9.5 gives an overview on additional analyses. Safety data are reported in the last section (9.6).

In most frequency tables the number of missing data is not shown although the calculation of percentages is based on all data including missing values (missing data are shown only if they exceed 5%). Therefore, percentages might not always sum to 100 %. Additionally, for binary variables only one category is shown (i.e. "yes" or "no" category, where appropriate).

9.1 Participants

The registry population comprised patients with hypertension and T2DM. Initially, it was planned to enroll 10,000 patients, but due to difficulties in enrolment, the sample size was reduced, i.e. the originally planned recruitment phase of approximately 10-12 months was extended to 19 months (see section 8.2).

Ultimately, 8,568 patients from 511 active sites were enrolled. Patients were followed-up at 6, 12, and 24 months after baseline visit. Figure 9-1 shows the number of documented patients used for the analysis per visit (baseline and follow-up visits). Numbers of documented follow-up visits at 24 months were particularly low (only about 50% of all enrolled patients had documented follow-up visits at 24 months), since not all patients had a 24-month follow-up visit (due to the fact that on 1st July 2014, the antidiabetics Galvus®/Eucreas® were withdrawn from the market, and thus, the registry and the documentation of follow-up visits was prematurely concluded in December 2014).

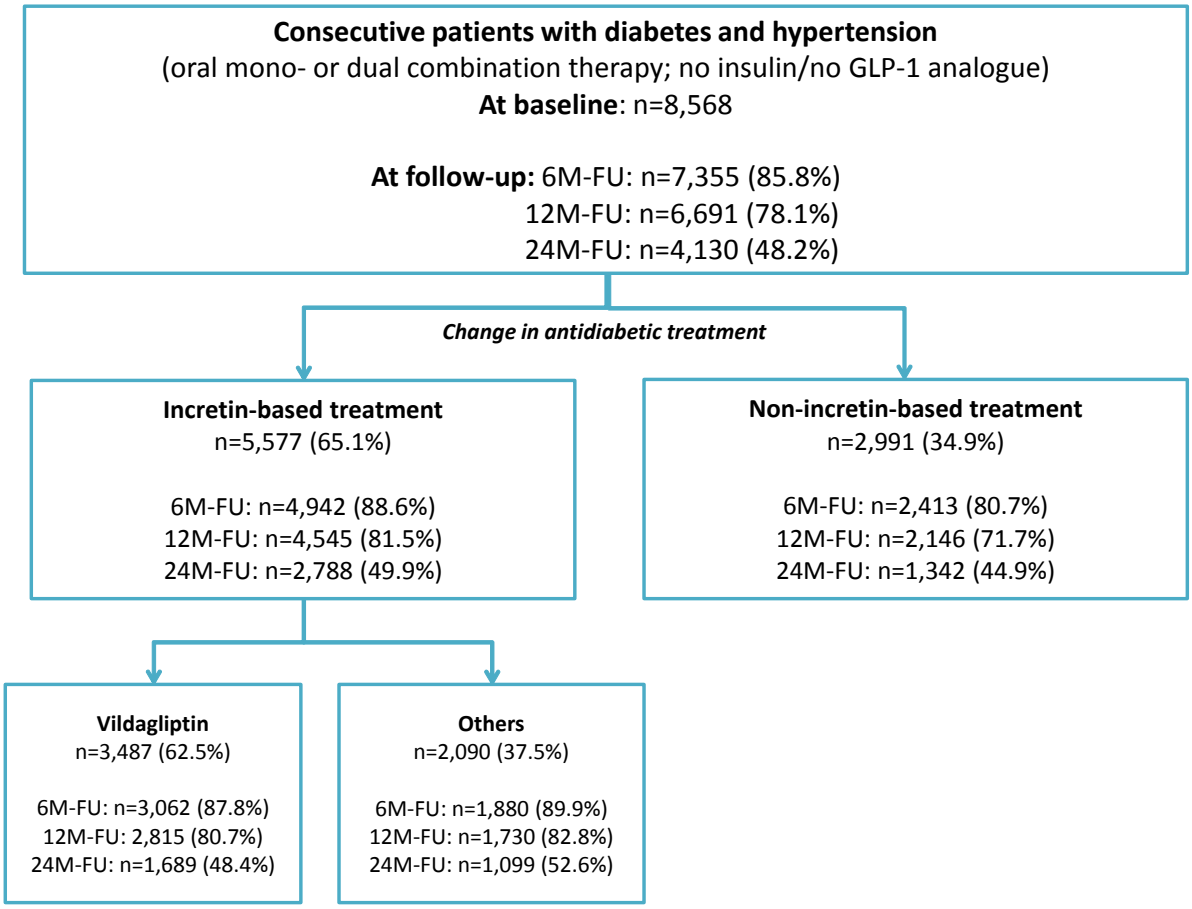

Figure 9-1. *Patient flow chart.*

9.2 Patient Characteristics

The data evaluation was performed for the total population and the three treatments groups

- Vildagliptin
- Other incretin-based treatment
- Non-incretin-based treatment

at baseline in comparison.

Overall, 8,568 hypertensive T2DM patients were enrolled at baseline. Among those 2,991 patients (34.9%) were initially treated with non-incretin-based medication and 5,577 patients with incretin-based medication. Among patients with incretin-based therapy, 3,487 (62.5%) patients were treated with vildagliptin and 2,090 (37.5%) with other incretin-based medication (Figure 9-1).

The complete descriptive statistical report regarding the comparison of the three treatment groups is given in Appendix 5.

Table 9-1 shows patient characteristics in the three treatment groups at baseline (i.e. Gender; Age; Blood pressure at admission; Heart rate; Weight; Height; Body-Mass-Index; Waist circumference; Level of care needed; Social status; Education; Smoking status and alcohol consumption; Physical exercise).

Table 9-2 shows comorbid diseases in the three treatment groups at baseline (i.e. Vascular concomitant diseases; Other diabetes-related diseases; History of amputation; Other concomitant diseases).

Table 9-3 shows available laboratory values at baseline (not older than 6 weeks) in the three treatment groups (i.e. Cholesterol; Glucose; Haemoglobin; Creatinine; Liver function)

Table 9-4 shows previous anti-diabetic therapy in the three treatment groups before baseline (i.e. Metformin; Sulfonylurea drugs; Glucosidase inhibitors; Glinides; Glitazones; DPP-4 inhibitors; SGTL-2 inhibitors; Novartis drugs).

Table 9-5 shows the reasons for pharmacotherapy change in the three treatment groups at baseline.

Table 9-6 shows current anti-diabetic therapy in the three treatment groups at baseline (i.e. Metformin; Sulfonylurea drugs; Glucosidase inhibitors; Glinides; Glitazones; DPP-4 inhibitors; GLP-1 analogs; SGTL-2 inhibitors; Total number of antidiabetics; Insulin; Novartis drugs).

Table 9-7 shows current anti-hypertensive therapy in the three treatment groups at baseline (i.e. ACE inhibitors; ARB; Direct renin inhibitor; Beta-blocker; Calcium channel blocker; Diuretic drugs; Total number of antihypertensive drugs; Fixed-dose combinations; Novartis drugs).

Table 9-8 shows other current medication in the three treatment groups at baseline.

Table 9-9 shows hypoglycemic events in the three treatment groups before baseline (i.e. Number of events; Type of events; Help needed).

Table 9-10 shows patient reported outcomes regarding diabetes and hypertension in the three treatment groups at baseline (i.e. Impact on weight; Symptoms; Continuity of medication; Number of tablets).

Table 9-11 shows Quality of Life data (EQ-5D) in the three treatment groups at baseline (i.e. Mobility; Self-care; Usual activities; Pain/discomfort; Anxiety/depression; Health status; EQoL-5D score).

Table 9-1. *Patient characteristics in the three treatment groups at baseline.*

Es wurden keine Einträge für das Inhaltsverzeichnis gefunden.	TOTAL	Vildagliptin	Incretin-based therapy	Non-incretin-based therapy	P-value
No. of patients	8568 (100.0 %)	3487 (40.7 %)	2090 (24.4 %)	2991 (34.9 %)	
Sociodemographics					
Women	45.5 % (3897/8567)	45.2 % (1577/3487)	45.9 % (959/2090)	45.5 % (1361/2990)	0.89081
Age at baseline [years]	65.08 ± 11.34	64.52 ± 11.52	64.22 ± 11.15	66.33 ± 11.17	<.00001
MEDIAN	65 (57, 74)	65 (56, 74)	64 (57, 73)	67 (58, 75)	
RANGE	19 , 97	19 , 96	27 , 94	20 , 97	
Age > 75yrs	19.7 % (1689/8567)	19.0 % (661/3487)	17.3 % (362/2090)	22.3 % (666/2990)	0.00002
Systolic blood pressure at admission	140.30 ± 15.71	140.46 ± 15.47	139.98 ± 15.97	140.33 ± 15.82	0.38580
Median	140.0 (130.0, 150.0)	140.0 (130.0, 150.0)	140.0 (130.0, 150.0)	140.0 (130.0, 150.0)	
RANGE	90.0 , 250.0	95.0 , 214.0	94.0 , 220.0	90.0 , 250.0	
[SBP - target]	5.81 ± 15.24	5.94 ± 15.11	5.44 ± 15.51	5.93 ± 15.21	0.41187
Diastolic blood pressure at admission	82.61 ± 9.46	82.87 ± 9.34	82.56 ± 9.68	82.33 ± 9.44	0.06771
Median	80.0 (80.0, 90.0)	80.0 (80.0, 90.0)	80.0 (80.0, 90.0)	80.0 (80.0, 90.0)	
RANGE	30.0 , 140.0	35.0 , 140.0	40.0 , 137.0	30.0 , 120.0	
[DBP - target]	-0.96 ± 9.50	-0.73 ± 9.41	-1.11 ± 9.74	-1.14 ± 9.44	0.15267
Heart rate [/min]	75.04 ± 10.02	74.94 ± 9.42	75.19 ± 10.12	75.05 ± 10.64	0.67920
Median	74.0 (68.0, 80.0)	74.0 (68.0, 80.0)	74.0 (68.0, 80.0)	74.0 (68.0, 80.0)	
RANGE	33.0 , 144.0	33.0 , 122.0	48.0 , 137.0	48.0 , 144.0	
Weight [kg]	90.36 ± 18.51	90.80 ± 18.03	92.40 ± 19.81	88.30 ± 17.90	<.00001
Median	88.0 (78.0, 100.0)	89.0 (80.0, 100.0)	90.0 (79.0, 103.0)	86.0 (76.0, 98.0)	
RANGE	43.0 , 203.0	43.0 , 200.0	45.0 , 192.0	43.0 , 203.0	
Height [cm]	170.03 ± 9.18	170.10 ± 9.06	170.30 ± 9.27	169.75 ± 9.26	0.17223
Median	170.0 (164.0, 176.0)	170.0 (164.0, 176.0)	170.0 (164.0, 177.0)	170.0 (163.0, 176.0)	
RANGE	104.0 , 200.0	128.0 , 198.0	137.0 , 200.0	104.0 , 198.0	
BMI [kg/m2]	31.22 ± 5.84	31.36 ± 5.75	31.81 ± 6.15	30.62 ± 5.66	<.00001
Median	30.1 (27.2, 34.3)	30.4 (27.5, 34.4)	30.6 (27.6, 35.2)	29.7 (26.7, 33.5)	
RANGE	15.8 , 85.1	18.1 , 70.0	17.4 , 60.8	15.8 , 85.1	
BMI < 25	10.2 % (859/8397)	9.1 % (316/3481)	8.9 % (186/2089)	12.6 % (357/2827)	<.00001

Es wurden keine Einträge für das Inhaltsverzeichnis gefunden.	TOTAL	Vildagliptin	Incretin-based therapy	Non-incretin-based therapy	P-value
BMI: 25 - 30	37.7 % (3165/8397)	37.8 % (1315/3481)	36.1 % (755/2089)	38.7 % (1095/2827)	0.17777
BMI > 30	52.1 % (4373/8397)	53.1 % (1850/3481)	55.0 % (1148/2089)	48.6 % (1375/2827)	0.00002
Waist circumference [cm]	107.65 ± 14.40	107.73 ± 13.50	109.22 ± 14.81	106.15 ± 14.98	<.00001
Median	106.0 (98.0, 116.0)	107.0 (99.0, 115.0)	108.0 (100.0, 118.0)	105.0 (96.0, 115.0)	
RANGE	62.0 , 190.0	66.0 , 175.0	62.0 , 190.0	64.0 , 174.0	
Known diabetes [years]	6.90 ± 5.63	6.82 ± 5.45	7.38 ± 6.00	6.64 ± 5.55	<.00001
Participation in diabetes training	72.1 % (6054/8399)	72.7 % (2533/3483)	75.4 % (1576/2090)	68.8 % (1945/2826)	<.00001
Participation in DMP for diabetes	85.2 % (7159/8401)	85.4 % (2975/3483)	85.6 % (1788/2090)	84.7 % (2396/2828)	0.65782
Health insurance	98.1 % (8402/8568)	99.9 % (3483/3487)	100.0 % (2090/2090)	94.6 % (2829/2991)	<.00001
Statutory health insurance	96.3 % (8087/8402)	96.0 % (3344/3483)	95.1 % (1987/2090)	97.4 % (2756/2829)	0.00006
Private health insurance	3.7 % (315/8402)	4.0 % (139/3483)	4.9 % (103/2090)	2.6 % (73/2829)	0.00006
In need of care	2.6 % (219/8395)	2.5 % (86/3477)	2.0 % (42/2090)	3.2 % (91/2828)	0.02556
Level 1 of care	84.9 % (186/219)	86.0 % (74/86)	88.1 % (37/42)	82.4 % (75/91)	0.65005
Level 2 of care	13.7 % (30/219)	14.0 % (12/86)	11.9 % (5/42)	14.3 % (13/91)	0.92980
Level 3 of care	1.4 % (3/219)	0.0 % (0/86)	0.0 % (0/42)	3.3 % (3/91)	0.11775
Social status					
Employed	30.7 % (2578/8398)	32.2 % (1121/3480)	33.1 % (692/2090)	27.1 % (765/2828)	<.00001
Economically inactive	64.1 % (5386/8398)	63.0 % (2192/3480)	61.9 % (1294/2090)	67.2 % (1900/2828)	0.00013
Unemployed	13.1 % (703/5386)	14.5 % (317/2192)	12.9 % (167/1294)	11.5 % (219/1900)	0.02065
Housewife/househusband	4.9 % (262/5386)	5.3 % (117/2192)	5.9 % (76/1294)	3.6 % (69/1900)	0.00626
Retirement	81.1 % (4368/5386)	79.4 % (1740/2192)	79.7 % (1031/1294)	84.1 % (1597/1900)	0.00023
Incapable of working	1.0 % (53/5386)	0.8 % (18/2192)	1.5 % (20/1294)	0.8 % (15/1900)	0.06320
Other status	0.7 % (62/8398)	0.7 % (26/3480)	0.9 % (19/2090)	0.6 % (17/2828)	0.45802
Status unknown	4.4 % (372/8398)	4.1 % (141/3480)	4.1 % (85/2090)	5.2 % (146/2828)	0.06678
Patient lives alone	20.4 % (1712/8381)	19.0 % (662/3478)	20.9 % (437/2090)	21.8 % (613/2813)	0.02156
Education					
1-8 years at school	31.4 % (2638/8395)	31.2 % (1086/3478)	30.8 % (644/2090)	32.1 % (908/2827)	0.58889

Es wurden keine Einträge für das Inhaltsverzeichnis gefunden.	TOTAL	Vildagliptin	Incretin-based therapy	Non-incretin-based therapy	P-value
9-12 years at school	23.6 % (1980/8395)	24.1 % (839/3478)	23.4 % (490/2090)	23.0 % (651/2827)	0.58621
Commercial / technical school	7.8 % (654/8395)	7.4 % (258/3478)	9.9 % (207/2090)	6.7 % (189/2827)	0.00010
University	4.3 % (358/8395)	4.2 % (145/3478)	4.9 % (102/2090)	3.9 % (111/2827)	0.24526
Unknown	32.9 % (2765/8395)	33.1 % (1150/3478)	31.0 % (647/2090)	34.2 % (968/2827)	0.05201
Smoker	11.7 % (978/8376)	11.0 % (382/3477)	11.9 % (249/2090)	12.4 % (347/2809)	0.22689
Ex-smoker	15.2 % (1274/8376)	15.0 % (522/3477)	16.7 % (349/2090)	14.3 % (403/2809)	0.06999
Non-smoker	73.1 % (6124/8376)	74.0 % (2573/3477)	71.4 % (1492/2090)	73.3 % (2059/2809)	0.09982
Alcohol consumption	61.8 % (5170/8371)	63.0 % (2191/3477)	62.7 % (1310/2090)	59.5 % (1669/2804)	0.01106
Monthly	47.0 % (2429/5170)	47.3 % (1037/2191)	45.3 % (594/1310)	47.8 % (798/1669)	0.37136
Weekly	40.4 % (2087/5170)	41.0 % (898/2191)	41.2 % (540/1310)	38.9 % (649/1669)	0.32183
Daily	12.6 % (654/5170)	11.7 % (256/2191)	13.4 % (176/1310)	13.3 % (222/1669)	0.19975
Physical exercise					
less than 1 hour/week	33.5 % (2806/8378)	33.4 % (1161/3480)	33.5 % (700/2090)	33.7 % (945/2808)	0.97074
1 hour/week	18.1 % (1518/8378)	18.0 % (628/3480)	18.2 % (380/2090)	18.2 % (510/2808)	0.98924
2 hours/week	17.9 % (1498/8378)	18.2 % (633/3480)	17.6 % (367/2090)	17.7 % (498/2808)	0.81328
3 hours/week	13.2 % (1105/8378)	13.6 % (475/3480)	14.0 % (292/2090)	12.0 % (338/2808)	0.08144
4 hours/week	7.0 % (588/8378)	7.0 % (242/3480)	7.0 % (146/2090)	7.1 % (200/2808)	0.96456
5 hours/week	4.0 % (333/8378)	3.9 % (135/3480)	3.8 % (80/2090)	4.2 % (118/2808)	0.74742
6 hours/week	2.1 % (178/8378)	2.1 % (72/3480)	2.1 % (44/2090)	2.2 % (62/2808)	0.92801
7 hours/week	1.6 % (134/8378)	1.6 % (55/3480)	1.1 % (24/2090)	2.0 % (55/2808)	0.08155
8 hours/week	0.7 % (60/8378)	0.5 % (16/3480)	0.7 % (15/2090)	1.0 % (29/2808)	0.02765
9 or more hours/week	1.9 % (158/8378)	1.8 % (63/3480)	2.0 % (42/2090)	1.9 % (53/2808)	0.86929

Table 9-2. *Comorbid diseases in the three treatment groups.*

	TOTAL	Vildagliptin	Incretin-based therapy	Non-incretin-based therapy	P-value
Vascular concomitant diseases	34.2 % (2928/8568)	33.6 % (1173/3487)	33.4 % (699/2090)	35.3 % (1056/2991)	0.26705
Coronary Heart Disease	23.9 % (1996/8356)	21.7 % (755/3479)	22.1 % (461/2090)	28.0 % (780/2787)	<.00001
History of myocardial infarction	8.3 % (696/8354)	8.0 % (279/3478)	8.8 % (183/2090)	8.4 % (234/2786)	0.62300
History of PCI	6.7 % (556/8351)	6.4 % (224/3478)	7.6 % (159/2090)	6.2 % (173/2783)	0.12422
History of CABG	3.6 % (299/8352)	3.6 % (124/3478)	3.6 % (75/2090)	3.6 % (100/2784)	0.99811
History of stroke/TIA	6.1 % (509/8352)	6.0 % (208/3478)	6.2 % (129/2090)	6.2 % (172/2784)	0.93465
Heart Failure	13.4 % (1119/8353)	12.9 % (450/3478)	13.5 % (282/2090)	13.9 % (387/2785)	0.53680
NYHA I	34.7 % (388/1118)	35.9 % (161/449)	34.8 % (98/282)	33.3 % (129/387)	0.74649
NYHA II	58.1 % (649/1118)	57.7 % (259/449)	56.7 % (160/282)	59.4 % (230/387)	0.76816
NYHA III	6.5 % (73/1118)	5.6 % (25/449)	7.1 % (20/282)	7.2 % (28/387)	0.56489
NYHA IV	0.7 % (8/1118)	0.9 % (4/449)	1.4 % (4/282)	0.0 % (0/387)	0.08440
Peripheral arterial occlusive disease	6.8 % (568/8352)	6.3 % (218/3478)	7.6 % (159/2090)	6.9 % (191/2784)	0.15565
Other and/or diabetes-related diseases	84.9 % (7271/8568)	87.5 % (3051/3487)	90.0 % (1881/2090)	78.2 % (2339/2991)	<.00001
Dyslipidemia	57.8 % (4828/8355)	58.1 % (2021/3481)	61.8 % (1290/2089)	54.5 % (1517/2785)	<.00001
Autonomous neuropathy	12.7 % (1061/8362)	12.3 % (428/3481)	14.8 % (309/2089)	11.6 % (324/2792)	0.00276
Non-proliferative diabetic retinopathy	4.2 % (352/8371)	3.8 % (133/3481)	4.3 % (90/2089)	4.6 % (129/2801)	0.29425
Proliferative diabetic retinopathy / laser coagulation	1.1 % (90/8369)	1.0 % (36/3480)	1.2 % (25/2089)	1.0 % (29/2800)	0.82475
Diabetic macular edema	0.8 % (65/7970)	0.6 % (20/3315)	1.0 % (19/1998)	1.0 % (26/2657)	0.20480
Ophthalmologist consultation	71.1 % (5954/8370)	72.5 % (2523/3479)	73.7 % (1539/2089)	67.5 % (1892/2802)	<.00001
Blindness	0.4 % (30/8383)	0.3 % (10/3481)	0.3 % (7/2089)	0.5 % (13/2813)	0.50293
Dialysis	0.1 % (9/8385)	0.1 % (4/3481)	0.1 % (2/2090)	0.1 % (3/2814)	0.97766
History of amputation	0.5 % (47/8568)	0.5 % (19/3487)	0.6 % (12/2090)	0.5 % (16/2991)	0.98209
Foot	14.9 % (7/47)	10.5 % (2/19)	16.7 % (2/12)	18.8 % (3/16)	0.77748
Toes	57.4 % (27/47)	63.2 % (12/19)	58.3 % (7/12)	50.0 % (8/16)	0.73333
Lower extremities	25.5 % (12/47)	26.3 % (5/19)	33.3 % (4/12)	18.8 % (3/16)	0.67796

	TOTAL	Vildagliptin	Incretin-based therapy	Non-incretin-based therapy	P-value
Upper extremities	6.4 % (3/47)	5.3 % (1/19)	0.0 % (0/12)	12.5 % (2/16)	0.39456
Other concomitant diseases	46.1 % (3856/8368)	47.8 % (1664/3482)	48.8 % (1020/2089)	41.9 % (1172/2797)	<.00001

Table 9-3. *Available laboratory values at baseline (last six weeks) in the three treatment groups.*

	TOTAL	Vildagliptin	Incretin-based therapy	Non-incretin-based therapy	P-value
No. of patients	8568 (100.0 %)	3487 (40.7 %)	2090 (24.4 %)	2991 (34.9 %)	
Total fasting cholesterol available	82.9 % (7099/8568)	84.1 % (2934/3487)	82.4 % (1722/2090)	81.7 % (2443/2991)	0.02612
Total fasting cholesterol [mmol/L]	5.31 ± 1.21	5.31 ± 1.24	5.24 ± 1.22	5.37 ± 1.18	0.00066
Fasting HDL-cholesterol available	70.4 % (6032/8568)	70.2 % (2449/3487)	70.9 % (1482/2090)	70.2 % (2101/2991)	0.84286
Fasting HDL-cholesterol [mmol/L]	1.26 ± 0.40	1.26 ± 0.41	1.23 ± 0.39	1.28 ± 0.40	0.00005
Fasting LDL-cholesterol available	69.9 % (5987/8568)	69.9 % (2438/3487)	70.4 % (1472/2090)	69.4 % (2077/2991)	0.74967
Fasting LDL-cholesterol [mmol/L]	3.20 ± 1.01	3.20 ± 1.00	3.15 ± 1.02	3.24 ± 1.02	0.03030
Fasting triglycerides available	74.0 % (6340/8568)	74.1 % (2584/3487)	74.5 % (1558/2090)	73.5 % (2198/2991)	0.68677
Fasting triglycerides [mmol/L]	2.32 ± 1.64	2.28 ± 1.51	2.45 ± 1.95	2.27 ± 1.53	0.01315
Fasting glucose available	83.1 % (7119/8568)	85.5 % (2982/3487)	83.1 % (1736/2090)	80.3 % (2401/2991)	<.00001
Fasting glucose [mmol/L]	8.51 ± 2.78	8.61 ± 2.73	8.76 ± 2.77	8.21 ± 2.82	<.00001
Postprandial glucose available	48.8 % (4178/8568)	49.8 % (1737/3487)	52.5 % (1097/2090)	44.9 % (1344/2991)	<.00001
Postprandial glucose [mmol/L]	10.87 ± 3.40	11.03 ± 3.32	11.00 ± 3.44	10.55 ± 3.45	0.00003
Hb1Ac available	94.5 % (8099/8568)	96.3 % (3358/3487)	96.9 % (2026/2090)	90.8 % (2715/2991)	<.00001
HbA1c [%]	7.80 ± 2.13	7.90 ± 2.84	7.92 ± 1.38	7.59 ± 1.42	<.00001
Haemoglobin available	60.2 % (5161/8568)	62.2 % (2168/3487)	60.3 % (1260/2090)	57.9 % (1733/2991)	0.00242
Haemoglobin [mmol/L]	8.26 ± 1.45	8.24 ± 1.50	8.24 ± 1.44	8.30 ± 1.40	0.56851
Serum creatinine available	82.5 % (7067/8568)	84.3 % (2940/3487)	82.9 % (1732/2090)	80.1 % (2395/2991)	0.00004
Serum creatinine [µmol/l]	85.53 ± 56.93	84.49 ± 48.87	86.89 ± 64.41	85.81 ± 60.25	0.25251
eGFR according to MDRD formula [ml/min]	81.81 ± 24.52	82.32 ± 24.03	82.00 ± 24.84	81.04 ± 24.87	0.03515
Microalbustix albumin [mg/l]	32.25 ± 37.50	30.98 ± 36.91	35.65 ± 40.92	30.32 ± 34.17	0.03863
Microalbustix creatinine [mg/dl]	56.83 ± 77.41	49.72 ± 72.55	64.46 ± 84.17	58.59 ± 76.42	0.01099
Macroalbuminuria: positive test	10.5 % (588/5615)	9.5 % (224/2367)	11.9 % (164/1380)	10.7 % (200/1868)	0.06043
Macroalbuminuria: negative test	89.5 % (5027/5615)	90.5 % (2143/2367)	88.1 % (1216/1380)	89.3 % (1668/1868)	0.06043
Increased liver function readings	19.6 % (1237/6304)	19.7 % (524/2664)	22.4 % (346/1548)	17.5 % (367/2092)	0.00147

Table 9-4. *Previous antidiabetic therapy in the three treatment groups before baseline.*

	TOTAL	Vildagliptin	Incretin-based therapy	Non-incretin-based therapy	P-value
No. of patients	8568 (100.0 %)	3487 (40.7 %)	2090 (24.4 %)	2991 (34.9 %)	
Metformin	79.9 % (6686/8373)	85.5 % (2981/3487)	84.0 % (1755/2090)	69.7 % (1950/2796)	<.00001
Metformin, dosage [mg/day]	1618.04 ± 582.18	1663.86 ± 543.97	1728.21 ± 523.87	1447.35 ± 648.68	<.00001
Duration of metformin treatment [yrs]	3.2 (1.4, 6.1)	3.1 (1.4, 6.0)	3.5 (1.5, 6.3)	3.2 (1.2, 6.1)	0.00087
Sulfonylurea drugs	23.9 % (1999/8362)	22.4 % (780/3483)	24.6 % (513/2089)	25.3 % (706/2790)	0.01963
Sulfonylurea drugs, dosage [mg/day]	3.40 ± 1.91	3.36 ± 1.81	3.40 ± 1.91	3.44 ± 2.01	0.94204
Duration of sulfonylurea treatment [yrs]	3.5 (1.6, 6.3)	3.7 (1.7, 6.4)	3.9 (1.7, 6.7)	3.1 (1.3, 5.8)	0.00024
Substance					
Carbutamide	0.0 % (0/1999)	0.0 % (0/780)	0.0 % (0/513)	0.0 % (0/706)	
Tolbutamide	0.0 % (0/1999)	0.0 % (0/780)	0.0 % (0/513)	0.0 % (0/706)	
Glibenclamide	25.5 % (509/1999)	23.5 % (183/780)	22.6 % (116/513)	29.7 % (210/706)	0.00483
Glibornuride	0.0 % (0/1999)	0.0 % (0/780)	0.0 % (0/513)	0.0 % (0/706)	
Gliclazide	0.1 % (1/1999)	0.0 % (0/780)	0.0 % (0/513)	0.1 % (1/706)	0.40004
Glipizide	0.0 % (0/1999)	0.0 % (0/780)	0.0 % (0/513)	0.0 % (0/706)	
Gliquidone	0.4 % (7/1999)	0.1 % (1/780)	0.6 % (3/513)	0.4 % (3/706)	0.36355
Glisoxepide	0.0 % (0/1999)	0.0 % (0/780)	0.0 % (0/513)	0.0 % (0/706)	
Glycodiazine	0.3 % (5/1999)	0.3 % (2/780)	0.0 % (0/513)	0.4 % (3/706)	0.34092
Glimepiride	73.2 % (1463/1999)	75.4 % (588/780)	76.2 % (391/513)	68.6 % (484/706)	0.00243
Other	0.7 % (14/1999)	0.8 % (6/780)	0.6 % (3/513)	0.7 % (5/706)	0.92666
Glucosidase inhibitors	2.4 % (197/8361)	2.2 % (77/3484)	2.1 % (44/2089)	2.7 % (76/2788)	0.27981
Glucosidase inhibitors, dosage [mg/day]	146.57 ± 86.34	139.57 ± 80.92	131.20 ± 86.33	162.55 ± 90.14	0.15374
Duration of treatment with glucosidase inhibitors [yrs]	2.7 (1.1, 6.1)	3.9 (1.9, 8.3)	2.7 (1.0, 5.9)	1.7 (0.7, 3.6)	0.00036
Substance					

	TOTAL	Vildagliptin	Incretin-based therapy	Non-incretin-based therapy	P-value
Acarbose	92.4 % (182/197)	94.8 % (73/77)	84.1 % (37/44)	94.7 % (72/76)	0.06261
Miglitol	5.6 % (11/197)	5.2 % (4/77)	11.4 % (5/44)	2.6 % (2/76)	0.13090
Other	2.0 % (4/197)	0.0 % (0/77)	4.5 % (2/44)	2.6 % (2/76)	0.20878
Glinide	3.2 % (265/8356)	3.0 % (104/3485)	3.4 % (72/2090)	3.2 % (89/2781)	0.63300
Glinide, dosage [mg/day]	23.73 ± 73.24	22.86 ± 75.78	25.42 ± 73.85	23.39 ± 70.48	0.04898
Duration of glinide treatment [yrs]	2.6 (1.1, 5.5)	3.2 (1.3, 6.1)	2.5 (0.7, 4.5)	2.4 (1.4, 5.1)	0.31258
Substance					
Nateglinide	7.9 % (21/265)	8.7 % (9/104)	9.7 % (7/72)	5.6 % (5/89)	0.59344
Repaglinide	86.4 % (229/265)	88.5 % (92/104)	86.1 % (62/72)	84.3 % (75/89)	0.69571
Other	5.7 % (15/265)	2.9 % (3/104)	4.2 % (3/72)	10.1 % (9/89)	0.07790
Glitazone	1.4 % (121/8362)	1.3 % (47/3485)	1.8 % (38/2089)	1.3 % (36/2788)	0.25431
Glitazone, dosage [mg/day]	30.81 ± 12.45	26.68 ± 13.23	32.95 ± 10.40	34.03 ± 12.18	0.01746
Duration of glitazone treatment [yrs]	3.8 (2.4, 5.4)	4.4 (2.8, 6.5)	3.4 (2.0, 4.8)	3.3 (1.9, 5.7)	0.04068
Substance					
Pioglitazon	87.5 % (105/120)	78.7 % (37/47)	92.1 % (35/38)	94.3 % (33/35)	0.06328
Other	12.5 % (15/120)	21.3 % (10/47)	7.9 % (3/38)	5.7 % (2/35)	0.06328
DPP-4 inhibitors	17.7 % (1482/8353)	18.5 % (644/3485)	31.3 % (654/2090)	6.6 % (184/2778)	<.00001
DPP-4 inhibitors, dosage [mg/day]	84.65 ± 35.18	84.68 ± 36.44	85.08 ± 34.47	83.02 ± 33.25	0.04617
Duration of DPP-4 inhibitor treatment [yrs]	1.4 (0.6, 2.4)	1.3 (0.4, 2.3)	1.6 (0.7, 2.5)	1.5 (0.6, 2.4)	0.00025
Substance					
Sitagliptin	49.1 % (727/1481)	19.1 % (123/644)	79.0 % (516/653)	47.8 % (88/184)	<.00001
Vildagliptin	44.6 % (660/1481)	78.6 % (506/644)	10.7 % (70/653)	45.7 % (84/184)	<.00001
Linagliptin	0.0 % (0/1481)	0.0 % (0/644)	0.0 % (0/653)	0.0 % (0/184)	
Saxagliptin	5.8 % (86/1481)	2.3 % (15/644)	9.3 % (61/653)	5.4 % (10/184)	<.00001
Other	0.5 % (8/1481)	0.0 % (0/644)	0.9 % (6/653)	1.1 % (2/184)	0.04362

	TOTAL	Vildagliptin	Incretin-based therapy	Non-incretin-based therapy	P-value
SGTL-2 inhibitors	0.2 % (16/8354)	0.2 % (6/3485)	0.3 % (6/2088)	0.1 % (4/2781)	0.49600
SGTL-2 inhibitors, dosage [mg/day]	17.56 ± 24.26	10.00 ± 0.00	24.33 ± 37.10	18.75 ± 20.97	0.98426
Duration of SGTL-2 inhibitor treatment [yrs]	0.3 (0.2, 0.8)	0.2 (0.1, 0.2)	0.3 (0.3, 1.2)	1.2 (0.4, 2.3)	0.04394
Substance					
Dapagliflozin	68.8 % (11/16)	100.0 % (6/6)	66.7 % (4/6)	25.0 % (1/4)	0.04279
Other	31.3 % (5/16)	0.0 % (0/6)	33.3 % (2/6)	75.0 % (3/4)	0.04279
Fixed-dose combination metformin / DPP-4 inhibitor	77.5 % (914/1179)	82.0 % (427/521)	74.2 % (388/523)	73.3 % (99/135)	0.00504
Novartis drugs					
Vildagliptin / Metformin					
Eucreas	85.7 % (396/462)	85.9 % (305/355)	84.6 % (44/52)	85.5 % (47/55)	0.96751
Icandra	14.3 % (66/462)	14.1 % (50/355)	15.4 % (8/52)	14.5 % (8/55)	0.96751
Vildagliptin					
Galvus	68.2 % (135/198)	68.2 % (103/151)	77.8 % (14/18)	62.1 % (18/29)	0.53164
Jalra	31.8 % (63/198)	31.8 % (48/151)	22.2 % (4/18)	37.9 % (11/29)	0.53164
Nateglinide					
STARLIX	95.2 % (20/21)	88.9 % (8/9)	100.0 % (7/7)	100.0 % (5/5)	0.49659
Other	4.8 % (1/21)	11.1 % (1/9)	0.0 % (0/7)	0.0 % (0/5)	0.49659

Table 9-5. *Reasons for pharmacotherapy change in the three treatment groups at baseline.*

	TOTAL	Vildagliptin	Incretin-based therapy	Non-incretin-based therapy	P-value
No. of patients	8568 (100.0 %)	3487 (40.7 %)	2090 (24.4 %)	2991 (34.9 %)	
Blood glucose adjustment	87.8 % (7329/8345)	89.1 % (3105/3484)	88.9 % (1857/2089)	85.4 % (2367/2772)	<.00001
Weight gain	19.8 % (1652/8345)	21.2 % (738/3484)	23.5 % (490/2089)	15.3 % (424/2772)	<.00001
Hypoglycemia	3.8 % (321/8345)	3.7 % (129/3484)	4.4 % (92/2089)	3.6 % (100/2772)	0.30443
Other reasons	19.0 % (1584/8345)	18.2 % (635/3484)	18.0 % (377/2089)	20.6 % (572/2772)	0.02464

Table 9-6. *Current antidiabetic therapy in the three treatment groups at baseline.*

	TOTAL	Vildagliptin	Incretin-based therapy	Non-incretin-based therapy	P-value
No. of patients	8568 (100.0 %)	3487 (40.7 %)	2090 (24.4 %)	2991 (34.9 %)	
Metformin	80.0 % (6682/8355)	81.6 % (2847/3487)	80.2 % (1675/2089)	77.7 % (2160/2779)	0.00058
Metformin, dosage [mg/day]	1711.80 ± 540.55	1783.51 ± 477.19	1810.60 ± 464.30	1539.68 ± 627.40	<.00001
Sulfonylurea drugs	17.5 % (1462/8351)	11.7 % (409/3484)	15.6 % (325/2088)	26.2 % (728/2779)	<.00001
Sulfonylurea drugs, dosage [mg/day]	3.21 ± 1.90	3.27 ± 1.86	3.09 ± 1.80	3.23 ± 1.96	0.38733
Substance					
Carbutamide	0.0 % (0/1461)	0.0 % (0/409)	0.0 % (0/325)	0.0 % (0/727)	
Tolbutamide	0.0 % (0/1461)	0.0 % (0/409)	0.0 % (0/325)	0.0 % (0/727)	
Glibenclamide	21.4 % (313/1461)	15.2 % (62/409)	13.8 % (45/325)	28.3 % (206/727)	<.00001
Glibornuride	0.0 % (0/1461)	0.0 % (0/409)	0.0 % (0/325)	0.0 % (0/727)	
Gliclazide	0.1 % (1/1461)	0.0 % (0/409)	0.0 % (0/325)	0.1 % (1/727)	0.60341
Glipizide	0.0 % (0/1461)	0.0 % (0/409)	0.0 % (0/325)	0.0 % (0/727)	
Gliquidone	0.3 % (5/1461)	0.2 % (1/409)	0.6 % (2/325)	0.3 % (2/727)	0.63078
Glisoxepide	0.1 % (2/1461)	0.2 % (1/409)	0.0 % (0/325)	0.1 % (1/727)	0.67302
Glycodiazine	1.2 % (18/1461)	1.7 % (7/409)	0.9 % (3/325)	1.1 % (8/727)	0.56805
Glimepiride	76.3 % (1115/1461)	82.6 % (338/409)	84.0 % (273/325)	69.3 % (504/727)	<.00001
Other	0.5 % (7/1461)	0.0 % (0/409)	0.6 % (2/325)	0.7 % (5/727)	0.25167
Glucosidase inhibitors	1.1 % (91/8354)	1.1 % (38/3485)	0.8 % (17/2088)	1.3 % (36/2781)	0.27891
Glucosidase inhibitors, dosage [mg/day]	151.62 ± 88.79	176.32 ± 85.22	144.12 ± 63.45	128.46 ± 97.86	0.01427
Substance					
Acarbose	91.1 % (82/90)	97.4 % (37/38)	94.1 % (16/17)	82.9 % (29/35)	0.08328
Miglitol	7.8 % (7/90)	2.6 % (1/38)	5.9 % (1/17)	14.3 % (5/35)	0.16908
Other	1.1 % (1/90)	0.0 % (0/38)	0.0 % (0/17)	2.9 % (1/35)	0.45179
Glinide	3.5 % (290/8342)	2.3 % (81/3484)	4.0 % (83/2089)	4.6 % (126/2769)	<.00001
Glinide, dosage [mg/day]	14.38 ± 56.32	13.73 ± 56.56	12.30 ± 55.11	16.16 ± 57.33	0.64940
Substance					
Nateglinide	2.8 % (8/290)	2.5 % (2/81)	2.4 % (2/83)	3.2 % (4/126)	0.93041
Repaglinide	94.1 % (273/290)	96.3 % (78/81)	95.2 % (79/83)	92.1 % (116/126)	0.40054

	TOTAL	Vildagliptin	Incretin-based therapy	Non-incretin-based therapy	P-value
Other	3.1 % (9/290)	1.2 % (1/81)	2.4 % (2/83)	4.8 % (6/126)	0.32855
Glitazone	0.5 % (43/8352)	0.1 % (4/3484)	0.3 % (7/2087)	1.2 % (32/2781)	<.00001
Glitazone, dosage [mg/day]	38.00 ± 22.38	21.25 ± 19.74	34.29 ± 18.80	41.00 ± 22.91	0.28411
Substance					
Pioglitazon	88.1 % (37/42)	100.0 % (4/4)	100.0 % (7/7)	83.9 % (26/31)	0.36532
Other	11.9 % (5/42)	0.0 % (0/4)	0.0 % (0/7)	16.1 % (5/31)	0.36532
DPP-4 inhibitors	62.5 % (5212/8342)	100.0 % (3487/3487)	82.5 % (1725/2090)	0.0 % (0/2765)	<.00001
DPP-4 inhibitors, dosage [mg/day]	84.81 ± 33.04	86.95 ± 31.51	80.48 ± 35.54	---	0.00256[U]
Substance					
Sitagliptin	28.4 % (1481/5211)	0.0 % (0/3487)	85.9 % (1481/1724)	---	<.00001
Vildagliptin	66.9 % (3487/5211)	100.0 % (3487/3487)	0.0 % (0/1724)	---	<.00001
Linagliptin	0.0 % (1/5211)	0.0 % (0/3487)	0.1 % (1/1724)	---	0.15493
Saxagliptin	4.3 % (222/5211)	0.0 % (0/3487)	12.9 % (222/1724)	---	<.00001
Other	0.4 % (20/5211)	0.0 % (0/3487)	1.2 % (20/1724)	---	<.00001
GLP-1 analogs/mimetics	4.8 % (404/8357)	0.5 % (18/3486)	18.5 % (386/2088)	0.0 % (0/2783)	<.00001
GLP-1 analogs/mimetics, dosage [mg/day]	6.27 ± 12.93	6.74 ± 11.65	6.25 ± 12.99	---	0.16857[U]
Substance					
Exenatide	43.9 % (177/403)	52.9 % (9/17)	43.5 % (168/386)	---	0.44383
Liraglutide	50.4 % (203/403)	41.2 % (7/17)	50.8 % (196/386)	---	0.43843
Other	5.7 % (23/403)	5.9 % (1/17)	5.7 % (22/386)	---	0.97462
SGTL-2 inhibitors	1.8 % (147/8358)	0.9 % (30/3486)	1.6 % (34/2088)	3.0 % (83/2784)	<.00001
SGTL-2 inhibitors, dosage [mg/day]	13.63 ± 16.38	12.93 ± 16.77	10.76 ± 7.06	15.06 ± 18.82	0.28032
Substance					
Dapagliflozin	95.2 % (138/145)	100.0 % (29/29)	97.1 % (33/34)	92.7 % (76/82)	0.24166
Other	4.8 % (7/145)	0.0 % (0/29)	2.9 % (1/34)	7.3 % (6/82)	0.24166
Total number of oral antidiabetics	1.71 ± 0.70	1.98 ± 0.52	2.03 ± 0.57	1.14 ± 0.61	<.00001
Median	2.0 (1.0, 2.0)	2.0 (2.0, 2.0)	2.0 (2.0, 2.0)	1.0 (1.0, 1.0)	
RANGE	0.0 , 5.0	1.0 , 5.0	1.0 , 4.0	0.0 , 3.0	

	TOTAL	Vildagliptin	Incretin-based therapy	Non-incretin-based therapy	P-value
None	3.9 % (328/8363)	0.0 % (0/3487)	0.0 % (0/2090)	11.8 % (328/2786)	<.00001
1 OAD	30.6 % (2555/8363)	14.1 % (492/3487)	13.9 % (290/2090)	63.6 % (1773/2786)	<.00001
2 OADs	56.1 % (4689/8363)	73.9 % (2576/3487)	69.4 % (1450/2090)	23.8 % (663/2786)	<.00001
>= 3 OADs	9.5 % (791/8363)	12.0 % (419/3487)	16.7 % (350/2090)	0.8 % (22/2786)	<.00001
Insulin(rapid-acting or long-acting or Pre-mixed)	15.1 % (1290/8568)	8.5 % (297/3487)	16.1 % (337/2090)	21.9 % (656/2991)	<.00001
Rapid-acting insulin	4.3 % (357/8360)	2.4 % (85/3485)	2.5 % (53/2088)	7.9 % (219/2787)	<.00001
Human insulin	50.1 % (179/357)	62.4 % (53/85)	52.8 % (28/53)	44.7 % (98/219)	0.02054
Analogues	49.9 % (178/357)	37.6 % (32/85)	47.2 % (25/53)	55.3 % (121/219)	0.02054
Syringe	3.4 % (12/357)	4.7 % (4/85)	0.0 % (0/53)	3.7 % (8/219)	0.30516
Pen	96.6 % (345/357)	95.3 % (81/85)	100.0 % (53/53)	96.3 % (211/219)	0.30516
Pump	0.0 % (0/357)	0.0 % (0/85)	0.0 % (0/53)	0.0 % (0/219)	
Other	0.0 % (0/357)	0.0 % (0/85)	0.0 % (0/53)	0.0 % (0/219)	
U-40	22.5 % (80/355)	32.1 % (27/84)	30.2 % (16/53)	17.0 % (37/218)	0.00646
U-100	77.5 % (275/355)	67.9 % (57/84)	69.8 % (37/53)	83.0 % (181/218)	0.00646
1x insulin/day	8.1 % (29/357)	12.9 % (11/85)	7.5 % (4/53)	6.4 % (14/219)	0.16982
2x insulin/day	16.0 % (57/357)	21.2 % (18/85)	18.9 % (10/53)	13.2 % (29/219)	0.19556
3x insulin/day	74.2 % (265/357)	63.5 % (54/85)	73.6 % (39/53)	78.5 % (172/219)	0.02699
4x insulin/day	1.7 % (6/357)	2.4 % (2/85)	0.0 % (0/53)	1.8 % (4/219)	0.55804
Long-acting insulin	12.6 % (1056/8361)	7.1 % (246/3486)	14.7 % (307/2089)	18.1 % (503/2786)	<.00001
Human insulin	30.0 % (317/1056)	29.3 % (72/246)	25.1 % (77/307)	33.4 % (168/503)	0.04148
Analogues	70.0 % (739/1056)	70.7 % (174/246)	74.9 % (230/307)	66.6 % (335/503)	0.04148
Syringe	5.8 % (61/1056)	6.5 % (16/246)	5.2 % (16/307)	5.8 % (29/503)	0.81088
Pen	93.8 % (991/1056)	92.7 % (228/246)	94.8 % (291/307)	93.8 % (472/503)	0.59214

	TOTAL	Vildagliptin	Incretin-based therapy	Non-incretin-based therapy	P-value
Pump	0.2 % (2/1056)	0.8 % (2/246)	0.0 % (0/307)	0.0 % (0/503)	0.03692
Other	0.2 % (2/1056)	0.0 % (0/246)	0.0 % (0/307)	0.4 % (2/503)	0.33238
U-40	16.3 % (171/1049)	22.0 % (53/241)	10.1 % (31/306)	17.3 % (87/502)	0.00066
U-100	83.7 % (878/1049)	78.0 % (188/241)	89.9 % (275/306)	82.7 % (415/502)	0.00066
1x insulin/day	88.1 % (930/1056)	91.9 % (226/246)	88.3 % (271/307)	86.1 % (433/503)	0.07131
2x insulin/day	10.1 % (107/1056)	6.5 % (16/246)	11.1 % (34/307)	11.3 % (57/503)	0.09774
3x insulin/day	1.6 % (17/1056)	1.2 % (3/246)	0.7 % (2/307)	2.4 % (12/503)	0.14027
4x insulin/day	0.2 % (2/1056)	0.4 % (1/246)	0.0 % (0/307)	0.2 % (1/503)	0.54927
Pre-mixed insulin	1.6 % (133/8360)	0.7 % (26/3485)	0.9 % (18/2089)	3.2 % (89/2786)	<.00001
Human insulin	56.4 % (75/133)	50.0 % (13/26)	61.1 % (11/18)	57.3 % (51/89)	0.73160
Analogues	43.6 % (58/133)	50.0 % (13/26)	38.9 % (7/18)	42.7 % (38/89)	0.73160
Syringe	4.5 % (6/133)	0.0 % (0/26)	0.0 % (0/18)	6.7 % (6/89)	0.21157
Pen	95.5 % (127/133)	100.0 % (26/26)	100.0 % (18/18)	93.3 % (83/89)	0.21157
Pump	0.0 % (0/133)	0.0 % (0/26)	0.0 % (0/18)	0.0 % (0/89)	
Other	0.0 % (0/133)	0.0 % (0/26)	0.0 % (0/18)	0.0 % (0/89)	
U-40	18.0 % (24/133)	11.5 % (3/26)	11.1 % (2/18)	21.3 % (19/89)	0.37044
U-100	82.0 % (109/133)	88.5 % (23/26)	88.9 % (16/18)	78.7 % (70/89)	0.37044
1x insulin/day	11.3 % (15/133)	11.5 % (3/26)	16.7 % (3/18)	10.1 % (9/89)	0.72435
2x insulin/day	83.5 % (111/133)	84.6 % (22/26)	77.8 % (14/18)	84.3 % (75/89)	0.78334
3x insulin/day	3.8 % (5/133)	0.0 % (0/26)	5.6 % (1/18)	4.5 % (4/89)	0.51970
4x insulin/day	1.5 % (2/133)	3.8 % (1/26)	0.0 % (0/18)	1.1 % (1/89)	0.51561
Fixed-dose combination metformin / DPP-4 inhibitor	73.6 % (3100/4210)	78.5 % (2236/2847)	63.4 % (864/1363)	---	<.00001
Novartis drugs					
Vildagliptin / Metformin					
Eucreas	91.9 % (2056/2236)	91.9 % (2056/2236)	---	---	

	TOTAL	Vildagliptin	Incretin-based therapy	Non-incretin-based therapy	P-value
Icandra	8.1 % (180/2236)	8.1 % (180/2236)	---	---	
Vildagliptin					
Galvus	86.8 % (1086/1251)	86.8 % (1086/1251)	---	---	
Jalra	13.2 % (165/1251)	13.2 % (165/1251)	---	---	
Nateglinide					
STARLIX	100.0 % (8/8)	100.0 % (2/2)	100.0 % (2/2)	100.0 % (4/4)	
Other	0.0 % (0/8)	0.0 % (0/2)	0.0 % (0/2)	0.0 % (0/4)	

Table 9-7. *Current anti-hypertensive therapy in the three treatment groups at baseline.*

	TOTAL	Vildagliptin	Incretin-based therapy	Non-incretin-based therapy	P-value
No. of patients	8568 (100.0 %)	3487 (40.7 %)	2090 (24.4 %)	2991 (34.9 %)	
ACE inhibitors	52.4 % (4377/8351)	52.1 % (1811/3476)	52.2 % (1090/2087)	52.9 % (1476/2788)	0.78786
ACE inhibitors, dosage [mg/day]	10.49 ± 12.67	10.32 ± 11.80	10.31 ± 11.69	10.85 ± 14.30	0.95011
Substance					
Captopril	2.7 % (116/4372)	2.0 % (36/1811)	2.3 % (25/1088)	3.7 % (55/1473)	0.00581
Enalapril	17.7 % (773/4372)	18.1 % (328/1811)	17.1 % (186/1088)	17.6 % (259/1473)	0.78016
Lisinopril	11.4 % (500/4372)	10.5 % (190/1811)	11.9 % (129/1088)	12.3 % (181/1473)	0.24164
Ramipril	65.4 % (2858/4372)	66.0 % (1196/1811)	66.1 % (719/1088)	64.0 % (943/1473)	0.40798
Trandolapril	0.1 % (6/4372)	0.2 % (4/1811)	0.2 % (2/1088)	0.0 % (0/1473)	0.21004
Other	2.7 % (119/4372)	3.1 % (57/1811)	2.5 % (27/1088)	2.4 % (35/1473)	0.34284
Angiotensin receptor blocker (ARB)	27.3 % (2281/8345)	29.0 % (1008/3476)	29.7 % (619/2087)	23.5 % (654/2782)	<.00001
ARB, dosage [mg/day]	115.32 ± 115.86	116.59 ± 121.49	114.58 ± 106.21	114.08 ± 115.90	0.90341
Substance					
Candesartan	22.9 % (522/2281)	24.1 % (243/1008)	24.4 % (151/619)	19.6 % (128/654)	0.05727
Irbesartan	5.7 % (130/2281)	6.0 % (60/1008)	5.3 % (33/619)	5.7 % (37/654)	0.87008
Losartan	7.9 % (181/2281)	8.8 % (89/1008)	4.0 % (25/619)	10.2 % (67/654)	0.00009
Valsartan	39.1 % (891/2281)	37.2 % (375/1008)	41.8 % (259/619)	39.3 % (257/654)	0.17475
Other	24.4 % (557/2281)	23.9 % (241/1008)	24.4 % (151/619)	25.2 % (165/654)	0.82898
Direct renin inhibitor	0.5 % (39/8343)	0.5 % (18/3475)	0.3 % (7/2087)	0.5 % (14/2781)	0.59153
Direct renin inhibitor, dosage [mg/day]	208.15 ± 93.96	217.56 ± 90.20	257.14 ± 73.19	171.57 ± 99.18	0.12534
Beta-blocker	46.5 % (3883/8351)	45.9 % (1596/3476)	47.6 % (994/2087)	46.4 % (1293/2788)	0.45771
Beta-blocker, dosage [mg/day]	53.25 ± 61.46	55.12 ± 61.98	54.78 ± 62.99	49.72 ± 59.48	0.01495
Substance					
Metoprolol	45.2 % (1754/3881)	47.1 % (752/1596)	44.5 % (442/994)	43.4 % (560/1291)	0.11548

	TOTAL	Vildagliptin	Incretin-based therapy	Non-incretin-based therapy	P-value
Bisoprolol	40.3 % (1563/3881)	39.3 % (627/1596)	40.3 % (401/994)	41.4 % (535/1291)	0.50143
Nebivolol	6.1 % (237/3881)	5.8 % (92/1596)	6.3 % (63/994)	6.4 % (82/1291)	0.75805
Carvedilol	4.7 % (182/3881)	4.3 % (69/1596)	5.5 % (55/994)	4.5 % (58/1291)	0.33726
Other	3.7 % (145/3881)	3.5 % (56/1596)	3.3 % (33/994)	4.3 % (56/1291)	0.36655
Calcium channel blocker	27.1 % (2257/8342)	28.1 % (976/3476)	29.3 % (612/2087)	24.1 % (669/2779)	0.00005
Calcium channel blocker, dosage [mg/day]	17.50 ± 41.24	17.83 ± 41.21	16.75 ± 41.48	17.72 ± 41.12	0.39455
Substance					
Amlodipine	75.2 % (1697/2256)	74.6 % (727/975)	78.6 % (481/612)	73.1 % (489/669)	0.06122
Nifedipine	2.7 % (60/2256)	2.4 % (23/975)	2.3 % (14/612)	3.4 % (23/669)	0.32740
Nisoldipine	0.0 % (1/2256)	0.1 % (1/975)	0.0 % (0/612)	0.0 % (0/669)	0.51829
Nimodipine	0.0 % (1/2256)	0.0 % (0/975)	0.0 % (0/612)	0.1 % (1/669)	0.30525
Diltiazem	0.6 % (13/2256)	0.5 % (5/975)	0.3 % (2/612)	0.9 % (6/669)	0.38032
Verapamil	3.2 % (73/2256)	3.5 % (34/975)	2.6 % (16/612)	3.4 % (23/669)	0.59485
Gallopamil	0.0 % (0/2256)	0.0 % (0/975)	0.0 % (0/612)	0.0 % (0/669)	
Felodipine	2.9 % (65/2256)	3.4 % (33/975)	2.5 % (15/612)	2.5 % (17/669)	0.45740
Nitrendipine	4.3 % (97/2256)	3.6 % (35/975)	4.4 % (27/612)	5.2 % (35/669)	0.26912
Lercanidipine	9.8 % (222/2256)	11.0 % (107/975)	8.7 % (53/612)	9.3 % (62/669)	0.26962
Nilvadipine	0.0 % (1/2256)	0.0 % (0/975)	0.0 % (0/612)	0.1 % (1/669)	0.30525
Manidipine	0.0 % (1/2256)	0.1 % (1/975)	0.0 % (0/612)	0.0 % (0/669)	0.51829
Isradipine	0.1 % (3/2256)	0.2 % (2/975)	0.0 % (0/612)	0.1 % (1/669)	0.54585
Other	1.0 % (22/2256)	0.7 % (7/975)	0.7 % (4/612)	1.6 % (11/669)	0.10944
Diuretic drugs	42.6 % (3556/8348)	44.4 % (1543/3476)	42.4 % (885/2087)	40.5 % (1128/2785)	0.00824
Diuretic drugs, dosage [mg/day]	18.8 (12.5, 25.0)	17.5 (12.5, 25.0)	20.0 (12.5, 25.0)	12.5 (12.5, 25.0)	0.00035
Substance					
Furosemide	8.4 % (298/3556)	7.8 % (120/1543)	8.1 % (72/885)	9.4 % (106/1128)	0.31357
Torasemide	22.8 % (810/3556)	20.9 % (322/1543)	21.7 % (192/885)	26.2 % (296/1128)	0.00321
Bumetanide	0.0 % (1/3556)	0.0 % (0/1543)	0.1 % (1/885)	0.0 % (0/1128)	0.22103
Etacrynic acid	0.0 % (1/3556)	0.0 % (0/1543)	0.1 % (1/885)	0.0 % (0/1128)	0.22103

	TOTAL	Vildagliptin	Incretin-based therapy	Non-incretin-based therapy	P-value
Piretanide	1.1 % (40/3556)	1.0 % (16/1543)	1.2 % (11/885)	1.2 % (13/1128)	0.89319
Hydrochlorothiazide	69.0 % (2452/3556)	72.3 % (1115/1543)	70.5 % (624/885)	63.2 % (713/1128)	<.00001
Clopamid	0.2 % (8/3556)	0.3 % (4/1543)	0.2 % (2/885)	0.2 % (2/1128)	0.90714
Other	8.2 % (293/3556)	7.6 % (117/1543)	9.3 % (82/885)	8.3 % (94/1128)	0.34542
Other anti-hypertensive therapy	10.2 % (849/8331)	9.1 % (315/3476)	9.6 % (201/2085)	12.0 % (333/2770)	0.00039
Total number of antihyper. Drugs	2.06 ± 1.15	2.09 ± 1.16	2.11 ± 1.12	2.00 ± 1.17	0.00052
Median	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)	
RANGE	0.0 , 6.0	0.0 , 6.0	0.0 , 6.0	0.0 , 6.0	
N	8352[N]	3476[N]	2087[N]	2789[N]	
None	6.5 % (542/8352)	5.8 % (201/3476)	5.1 % (107/2087)	8.4 % (234/2789)	<.00001
1 AHD	28.9 % (2411/8352)	29.4 % (1021/3476)	28.0 % (585/2087)	28.9 % (805/2789)	0.56438
2 AHDs	29.5 % (2460/8352)	28.7 % (996/3476)	30.1 % (629/2087)	29.9 % (835/2789)	0.39482
3 AHDs	23.9 % (1998/8352)	24.7 % (857/3476)	25.2 % (526/2087)	22.1 % (615/2789)	0.01597
>=4 AHDs	11.3 % (941/8352)	11.5 % (401/3476)	11.5 % (240/2087)	10.8 % (300/2789)	0.57924
Fixed-dose combinations					
Fixed-dose combination ARB/calcium channel blocker/diuretic	71.1 % (447/629)	72.5 % (219/302)	71.1 % (118/166)	68.3 % (110/161)	0.63821
Fixed-dose combination ACE inhibitor/diuretic	50.4 % (911/1808)	50.6 % (388/767)	50.9 % (223/438)	49.8 % (300/603)	0.92392
Fixed-dose combination ARB/diuretic	65.2 % (606/930)	67.9 % (281/414)	62.4 % (151/242)	63.5 % (174/274)	0.28811
Fixed-dose combination ARB/calcium channel blocker	37.9 % (186/491)	33.5 % (70/209)	43.9 % (68/155)	37.8 % (48/127)	0.13042
Fixed-dose combination ACE inhibitor/calcium channel blocker	14.2 % (153/1075)	16.2 % (74/457)	13.6 % (38/280)	12.1 % (41/338)	0.25128
Fixed-dose combination direct renin inhibitor/diuretic	56.5 % (13/23)	70.0 % (7/10)	50.0 % (3/6)	42.9 % (3/7)	0.50285
Novartis drugs					
Valsartan / Hydrochlorothiazide					
CoDiovan	32.1 % (69/215)	25.3 % (25/99)	46.6 % (27/58)	29.3 % (17/58)	0.01930
Codiovan forte	14.4 % (31/215)	9.1 % (9/99)	19.0 % (11/58)	19.0 % (11/58)	0.12119
Cordinate plus	1.4 % (3/215)	1.0 % (1/99)	1.7 % (1/58)	1.7 % (1/58)	0.90577
Provas	0.5 % (1/215)	1.0 % (1/99)	0.0 % (0/58)	0.0 % (0/58)	0.55511

	TOTAL	Vildagliptin	Incretin-based therapy	Non-incretin-based therapy	P-value
Provas comp	6.5 % (14/215)	7.1 % (7/99)	6.9 % (4/58)	5.2 % (3/58)	0.88877
Provas maxx	1.9 % (4/215)	3.0 % (3/99)	0.0 % (0/58)	1.7 % (1/58)	0.39704
Other	43.3 % (93/215)	53.5 % (53/99)	25.9 % (15/58)	43.1 % (25/58)	0.00333
Valsartan					
Cordinate	4.0 % (13/322)	3.9 % (5/128)	5.4 % (5/92)	2.9 % (3/102)	0.67511
Diovan	34.8 % (112/322)	33.6 % (43/128)	27.2 % (25/92)	43.1 % (44/102)	0.06185
Provas	7.1 % (23/322)	5.5 % (7/128)	5.4 % (5/92)	10.8 % (11/102)	0.22484
Valsartan / Amlodipine / Hydrochlorothiazide					
Exforge HCT	77.0 % (164/213)	80.9 % (76/94)	74.2 % (49/66)	73.6 % (39/53)	0.49180
Dafiro HCT	13.1 % (28/213)	11.7 % (11/94)	12.1 % (8/66)	17.0 % (9/53)	0.63283
Other	9.9 % (21/213)	7.4 % (7/94)	13.6 % (9/66)	9.4 % (5/53)	0.43045
Aliskiren					
Rasilez	96.2 % (25/26)	100.0 % (11/11)	100.0 % (4/4)	90.9 % (10/11)	0.49209
Other	3.8 % (1/26)	0.0 % (0/11)	0.0 % (0/4)	9.1 % (1/11)	0.49209
Hydrochlorothiazide					
Esidrix	3.8 % (23/606)	4.4 % (12/272)	3.2 % (5/156)	3.4 % (6/178)	0.77114
Other	96.2 % (583/606)	95.6 % (260/272)	96.8 % (151/156)	96.6 % (172/178)	0.77114
Aliskiren / Hydrochlorothiazide					
Rasilez HCT	92.3 % (12/13)	85.7 % (6/7)	100.0 % (3/3)	100.0 % (3/3)	0.62858
Other	7.7 % (1/13)	14.3 % (1/7)	0.0 % (0/3)	0.0 % (0/3)	0.62858
Valsartan / Amlodipine					
Exforge	79.2 % (84/106)	82.1 % (32/39)	84.2 % (32/38)	69.0 % (20/29)	0.26988
Dafiro	16.0 % (17/106)	15.4 % (6/39)	13.2 % (5/38)	20.7 % (6/29)	0.70032
Other	4.7 % (5/106)	2.6 % (1/39)	2.6 % (1/38)	10.3 % (3/29)	0.24494

Table 9-8. *Other current medication in the three treatment groups at baseline.*

	TOTAL	Vildagliptin	Incretin-based therapy	Non-incretin-based therapy	P-value
ASS	31.0 % (2583/8342)	31.0 % (1076/3476)	31.6 % (659/2087)	30.5 % (848/2779)	0.73019
Clopidogrel	2.9 % (241/8339)	2.6 % (90/3476)	3.2 % (66/2087)	3.1 % (85/2776)	0.37434
Prasugrel	0.2 % (18/8337)	0.3 % (9/3476)	0.1 % (3/2087)	0.2 % (6/2774)	0.66934
Ticagrelor	0.2 % (17/8337)	0.2 % (6/3476)	0.1 % (2/2087)	0.3 % (9/2774)	0.18771
Nitrates	2.4 % (200/8338)	2.4 % (84/3476)	2.5 % (52/2087)	2.3 % (64/2775)	0.91261
Oral anticoagulants	7.6 % (637/8340)	7.1 % (247/3477)	8.0 % (167/2087)	8.0 % (223/2776)	0.29930
Statins	41.3 % (3449/8346)	41.4 % (1438/3477)	43.8 % (914/2087)	39.4 % (1097/2782)	0.00926
Ezetimibe	2.9 % (238/8337)	3.3 % (116/3476)	3.2 % (67/2087)	2.0 % (55/2774)	0.00322
Other lipid lowering drugs	4.4 % (367/8336)	4.0 % (138/3473)	4.0 % (83/2087)	5.3 % (146/2776)	0.02653
Antidepressants	7.9 % (657/8340)	8.2 % (285/3477)	7.9 % (164/2087)	7.5 % (208/2776)	0.58995
Other	39.0 % (3248/8336)	39.6 % (1377/3475)	39.4 % (823/2087)	37.8 % (1048/2774)	0.29063

Table 9-9. *Hypoglycemic events in the three treatment groups before baseline.*

	TOTAL	Vildagliptin	Incretin-based therapy	Non-incretin-based therapy	P-value
Hypoglycemic events within last 12 months					
Without specific symptoms	3.5 % (282/8094)	3.2 % (106/3346)	3.2 % (64/2031)	4.1 % (112/2717)	0.08400
No. of events	3.68 ± 4.65	3.92 ± 5.92	4.30 ± 4.91	3.11 ± 2.82	0.27700
Symptomatic, but controllable without external help	3.8 % (314/8182)	3.7 % (124/3397)	3.9 % (79/2051)	4.1 % (111/2734)	0.70805
No. of events	3.79 ± 4.60	4.37 ± 4.99	4.11 ± 6.16	2.93 ± 2.15	0.05862
External help needed	0.7 % (54/8202)	0.5 % (17/3411)	0.5 % (11/2055)	1.0 % (26/2736)	0.06803
No. of events	2.81 ± 2.50	3.24 ± 2.11	3.55 ± 3.78	2.23 ± 2.01	0.18409
Symptomatic with medical help	0.7 % (55/8211)	0.8 % (26/3419)	0.4 % (8/2053)	0.8 % (21/2739)	0.19887
No. of events	4.04 ± 2.83	4.62 ± 2.38	5.00 ± 4.17	2.95 ± 2.54	0.01664
Hospitalization required	0.2 % (13/8257)	0.2 % (6/3439)	0.0 % (1/2063)	0.2 % (6/2755)	0.32304
No. of events	1.08 ± 0.28	1.17 ± 0.41	---	1.00 ± 0.00	0.55804

Table 9-10. *Patient reported outcomes regarding diabetes and hypertension in the three treatment groups at baseline.*

	TOTAL	Vildagliptin	Incretin-based therapy	Non-incretin-based therapy	P-value
No. of patients	8568 (100.0 %)	3487 (40.7 %)	2090 (24.4 %)	2991 (34.9 %)	
Antidiabetic therapy: impact on weight					
No change in weight	65.1 % (3282/5044)	64.7 % (1313/2029)	66.4 % (906/1364)	64.4 % (1063/1651)	0.46011
Weight gain	24.4 % (1233/5044)	24.8 % (503/2029)	23.3 % (318/1364)	25.0 % (412/1651)	0.51988
Weight loss	10.5 % (529/5044)	10.5 % (213/2029)	10.3 % (140/1364)	10.7 % (176/1651)	0.93927
Symptoms of hypoglycemia under antidiabetic medication					
No symptoms of hypoglycemia	85.3 % (4284/5021)	85.5 % (1734/2029)	86.1 % (1166/1354)	84.5 % (1384/1638)	0.44716
Once/twice symptoms of hypoglycemia	12.8 % (644/5021)	12.7 % (258/2029)	11.7 % (158/1354)	13.9 % (228/1638)	0.18321
Weekly symptoms of hypoglycemia	1.9 % (93/5021)	1.8 % (37/2029)	2.2 % (30/1354)	1.6 % (26/1638)	0.44368
Continuity of antidiabetic medication within last 12 months					
Continuous antidiabetic medication	71.8 % (3548/4941)	72.8 % (1455/1998)	71.1 % (948/1333)	71.1 % (1145/1610)	0.42555
Non-continuous antidiabetic medication	28.2 % (1393/4941)	27.2 % (543/1998)	28.9 % (385/1333)	28.9 % (465/1610)	0.42555
Continuity of antihypertensive medication within last 12 months					
Continuous antihypertensive medication	83.3 % (4090/4911)	82.7 % (1642/1986)	82.9 % (1095/1321)	84.4 % (1353/1604)	0.37127
Non-continuous antihypertensive medication	16.7 % (821/4911)	17.3 % (344/1986)	17.1 % (226/1321)	15.6 % (251/1604)	0.37127
No. of tablets for diabetes and hypertension					
1 - 3 tablets	48.1 % (2417/5021)	48.0 % (974/2028)	46.1 % (626/1358)	50.0 % (817/1635)	0.10688
4 - 6 tablets	42.4 % (2129/5021)	42.2 % (855/2028)	44.3 % (602/1358)	41.1 % (672/1635)	0.19704
7 or more tablets	9.5 % (475/5021)	9.8 % (199/2028)	9.6 % (130/1358)	8.9 % (146/1635)	0.65328

Table 9-11. *Quality of Life data (EQ-5D) in the three treatment groups at baseline.*

	TOTAL	Vildagliptin	Incretin-based therapy	Non-incretin-based therapy	P-value
No. of patients	8568 (100.0 %)	3487 (40.7 %)	2090 (24.4 %)	2991 (34.9 %)	
Mobility					
No problems	73.5 % (3704/5040)	73.0 % (1480/2027)	73.5 % (1002/1363)	74.1 % (1222/1650)	0.77429
Some problems	26.2 % (1322/5040)	26.6 % (539/2027)	26.3 % (358/1363)	25.8 % (425/1650)	0.84885
Confined to bed	0.3 % (14/5040)	0.4 % (8/2027)	0.2 % (3/1363)	0.2 % (3/1650)	0.42485
Self-care					
No problems	90.1 % (4535/5035)	90.1 % (1829/2031)	90.9 % (1235/1358)	89.4 % (1471/1646)	0.35647
Some problems	9.2 % (465/5035)	9.0 % (183/2031)	8.6 % (117/1358)	10.0 % (165/1646)	0.37397
Unable	0.7 % (35/5035)	0.9 % (19/2031)	0.4 % (6/1358)	0.6 % (10/1646)	0.20751
Usual activities					
No problems	76.9 % (3876/5038)	77.5 % (1573/2030)	76.8 % (1044/1359)	76.3 % (1259/1649)	0.71243
Some problems	21.9 % (1105/5038)	21.2 % (431/2030)	22.0 % (299/1359)	22.7 % (375/1649)	0.54446
Unable	1.1 % (57/5038)	1.3 % (26/2030)	1.2 % (16/1359)	0.9 % (15/1649)	0.56114
Pain/discomfort					
None	50.5 % (2538/5026)	49.2 % (995/2024)	50.4 % (683/1354)	52.2 % (860/1648)	0.18957
Moderate	45.6 % (2290/5026)	46.9 % (950/2024)	45.8 % (620/1354)	43.7 % (720/1648)	0.14222
Extreme	3.9 % (198/5026)	3.9 % (79/2024)	3.8 % (51/1354)	4.1 % (68/1648)	0.87554
Anxiety/depression					
Not anxious or depressed	72.9 % (3668/5034)	72.0 % (1465/2034)	72.5 % (982/1355)	74.2 % (1221/1645)	0.30587
Moderately anxious or depressed	24.6 % (1238/5034)	25.5 % (518/2034)	25.2 % (342/1355)	23.0 % (378/1645)	0.17771
Extremely anxious or depressed	2.5 % (128/5034)	2.5 % (51/2034)	2.3 % (31/1355)	2.8 % (46/1645)	0.67282
Health state today	72.0 (60.0, 82.0)	72.0 (60.0, 82.0)	70.5 (60.0, 82.0)	72.0 (60.0, 83.0)	0.87502
EQoL-D5 score acc. to Greiner, 2004	0.88 ± 0.18	0.87 ± 0.18	0.88 ± 0.17	0.88 ± 0.18	0.49082

9.3 Individualized Treatment Targets

The data evaluation was performed for the total population and the three treatment target groups based on

- Initial target HbA1c: ≤ 6.5% [strict] / >6.5 – 7.0% [medium] / >7.0 – ≤ 7.5% [loose]
- Initial target systolic BP: ≤ 130 mmHg [strict] / >130 – 135 mmHg [medium] / >135 – - ≤ 140 mmHg [loose]

at baseline in comparison.

The complete descriptive statistical report regarding the comparison of the treatment target groups (HbA1c; SBP) is given in Appendix 6.

Table 9-12 shows individualized therapy targets (regarding HbA1c and Blood pressure) in the three treatment groups at baseline.

Table 9-12. *Frequency distribution of individualized therapy targets in the three treatment groups at baseline.*

Es wurden keine Einträge für das Inhaltsverzeichnis gefunden.	TOTAL	Vildagliptin	Incretin-based therapy	Non-incretin-based therapy	P-value
HbA1c <= 6.5 [%]	39.0 % (3342/8567)	37.8 % (1318/3487)	36.0 % (753/2090)	42.5 % (1271/2990)	<.00001
HbA1c <= 7.0 [%]	42.3 % (3625/8567)	44.8 % (1561/3487)	45.3 % (946/2090)	37.4 % (1118/2990)	<.00001
HbA1c <= 7.5 [%]	18.7 % (1600/8567)	17.4 % (608/3487)	18.7 % (391/2090)	20.1 % (601/2990)	0.02323
Systolic blood pressure <= 130 mmHg	38.7 % (3319/8567)	38.3 % (1334/3487)	37.6 % (785/2090)	40.1 % (1200/2990)	0.13414
Systolic blood pressure <= 135 mmHg	33.3 % (2853/8567)	34.4 % (1198/3487)	35.2 % (735/2090)	30.8 % (920/2990)	0.00108
Systolic blood pressure <= 140 mmHg	27.6 % (2364/8567)	27.1 % (945/3487)	27.0 % (564/2090)	28.6 % (855/2990)	0.31469
Other value	0.4 % (34/8567)	0.4 % (13/3487)	0.3 % (6/2090)	0.5 % (15/2990)	0.46787
Other therapy target [mmHg]	152.70 ± 12.08	150.75 ± 15.03	152.33 ± 7.92	155.56 ± 10.44	0.26796

9.3.1 HbA1c treatment target groups

Table 9-13 shows multivariate predictors for a loose treatment target in the HbA1c treatment target groups (i.e. HbA1C target of >7.0 – ≤ 7.5%): factors assessed at baseline contributing to the assignment of patients into the loose target group for HbA1c.

Table 9-14 shows patient characteristics in the HbA1c treatment groups at baseline (i.e. Gender; Age; Blood pressure at admission; Heart rate; Weight; Height; Body-Mass-Index; Waist circumference; Level of care needed; Social status; Education; Smoking status and alcohol consumption; Physical exercise).

Table 9-15 shows comorbid diseases in the HbA1c treatment groups at baseline (i.e. Vascular concomitant diseases; Other diabetes-related diseases; History of amputation; Other concomitant diseases).

Table 9-16 shows available laboratory values at baseline (not older than 6 weeks) in the HbA1c treatment groups (i.e. Cholesterol; Glucose; Haemoglobin; Creatinine; Liver function)

Table 9-17 shows therapeutic patterns in the HbA1c treatment groups at baseline: previous antidiabetic therapy (i.e. Metformin; Sulfonylurea drugs; Glucosidase inhibitors; Glinide; Glitazone; DPP-4 inhibitors; SGTL-2 inhibitors; Novartis drugs).

Table 9-18 shows the reasons for pharmacotherapy change in the HbA1c treatment groups at baseline.

Table 9-19 shows therapeutic patterns in the HbA1c treatment groups at baseline: current anti-diabetic therapy (i.e. Metformin; Sulfonylurea drugs; Glucosidase inhibitors; Glinide; Glitazone; DPP-4 inhibitors; GLP-1 analogs; SGTL-2 inhibitors; Total number of antidiabetics; Insulin; Novartis drugs).

Table 9-20 shows therapeutic patterns in the HbA1c treatment groups at baseline: current anti-hypertensive therapy (i.e. ACE inhibitors; ARB; Direct renin inhibitor; Beta-blocker; Calcium channel blocker; Diuretic drugs; Total number of antihypertensive drugs; Fixed-dose combinations; Novartis drugs).

Table 9-21 shows hypoglycemic events in the HbA1c treatment groups before baseline (i.e. Number of events; Type of events; Help needed).

Table 9-22 shows patient reported outcomes regarding diabetes and hypertension in the HbA1c treatment groups at baseline (i.e. Impact on weight; Symptoms; Continuity of medication; Number of tablets).

Table 9-23 shows Quality of Life data (EQ-5D) in the HbA1c treatment groups at baseline (i.e. Mobility; Self-care; Usual activities; Pain/discomfort; Anxiety/depression; Health status; EQoL-5D score).

Table 9-13. *Multivariate adjusted predictors for choosing a loose treatment target (HbA1c >7.0% to ≤7.5%).*

	Odds Ratio Estimate	95% Confidence Interval	
Age (years) (≥ vs. < median)	**1.161**	**1.004**	**1.341**
Female sex (%)	1.025	0.896	1.172
BMI (kg/m^2) (≥ vs. < median)	0.999	0.873	1.145
Fasting blood glucose (mmol/l) (≥ vs. < median)	**1.427**	**1.230**	**1.656**
Current smoker (%)	0.922	0.748	1.136
Diabetes duration (years) (≥ vs. < median)	**1.359**	**1.188**	**1.554**
HbA1c (%)(≥ vs. < median)	**3.209**	**2.775**	**3.711**
Systolic BP (mmHg) (≥ vs. < median)	**1.194**	**1.044**	**1.364**
Prior myocardial infarction (yes vs. no)	0.911	0.715	1.160
Prior stroke/TIA (yes vs. no)	0.937	0.716	1.225
Heart failure (yes vs. no)	**1.368**	**1.134**	**1.652**
Peripheral arterial disease (yes vs. no)	**1.448**	**1.129**	**1.856**
Neuropathy (yes vs. no)	1.176	0.974	1.420
Non-proliferative diabetic retinopathy (yes vs. no)	0.760	0.550	1.051

Table 9-14. *Patient characteristics in the HbA1c treatment groups at baseline.*

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
No. of patients	8567 (100.0 %)	3342 (39.0 %)	3625 (42.3 %)	1600 (18.7 %)	
Sociodemographics					
Women	45.5 % (3897/8567)	46.2 % (1543/3342)	45.5 % (1649/3625)	44.1 % (705/1600)	0.37946
Age at baseline [years]	65.08 ± 11.34, n=8567	63.46 ± 11.86, n=3342	66.14 ± 10.72, n=3625	66.04 ± 11.23, n=1600	<.00001
MEDIAN	65 (57, 74)	64 (55, 73)	67 (59, 74)	66 (58, 75)	
RANGE	19 , 97	19 , 93	20 , 97	26 , 96	
Age > 75yrs	19.7 % (1689/8567)	17.7 % (592/3342)	20.5 % (743/3625)	22.1 % (354/1600)	0.00038
Systolic blood pressure at admission	140.30 ± 15.71, n=8398	139.43 ± 15.87, n=3306	140.69 ± 15.54, n=3583	141.26 ± 15.69, n=1509	<.00001
Median	140.0 (130.0, 150.0)	140.0 (130.0, 150.0)	140.0 (130.0, 150.0)	140.0 (130.0, 150.0)	
RANGE	90.0 , 250.0	90.0 , 223.0	95.0 , 250.0	94.0 , 220.0	
[SBP - target]	5.81 ± 15.24, n=8364	7.31 ± 15.52, n=3297	5.29 ± 15.24, n=3578	3.76 ± 14.29, n=1489	<.00001
Diastolic blood pressure at admission	82.61 ± 9.46, n=8397	82.40 ± 9.73, n=3305	82.66 ± 9.20, n=3583	82.95 ± 9.47, n=1509	0.01175
Median	80.0 (80.0, 90.0)	80.0 (79.0, 90.0)	80.0 (80.0, 90.0)	80.0 (80.0, 90.0)	
RANGE	30.0 , 140.0	30.0 , 140.0	42.0 , 120.0	38.0 , 120.0	
[DBP - target]	-0.96 ± 9.50, n=8397	0.69 ± 9.69, n=3305	-1.81 ± 9.32, n=3583	-2.56 ± 8.98, n=1509	<.00001
Heart rate [/min]	75.04 ± 10.02, n=8349	74.77 ± 10.37, n=3280	74.97 ± 9.45, n=3572	75.78 ± 10.51, n=1497	0.00061
Median	74.0 (68.0, 80.0)	73.0 (68.0, 80.0)	74.0 (68.0, 80.0)	76.0 (69.0, 80.0)	
RANGE	33.0 , 144.0	33.0 , 144.0	43.0 , 131.0	48.0 , 142.0	
Weight [kg]	90.36 ± 18.51, n=8403	90.13 ± 18.48, n=3309	90.42 ± 18.37, n=3582	90.69 ± 18.91, n=1512	0.76051
Median	88.0 (78.0, 100.0)	88.0 (78.0, 100.0)	88.0 (78.0, 100.0)	88.5 (78.0, 101.0)	
RANGE	43.0 , 203.0	45.0 , 199.0	47.0 , 203.0	43.0 , 200.0	
Height [cm]	170.03 ± 9.18, n=8399	170.17 ± 9.38, n=3307	169.95 ± 9.13, n=3580	169.93 ± 8.86, n=1512	0.54606
Median	170.0 (164.0, 176.0)	170.0 (164.0, 177.0)	170.0 (163.0, 176.0)	170.0 (164.0, 176.0)	
RANGE	104.0 , 200.0	104.0 , 198.0	128.0 , 200.0	140.0 , 197.0	
BMI [kg/m2]	31.22 ± 5.84, n=8397	31.10 ± 5.84, n=3307	31.27 ± 5.77, n=3580	31.37 ± 6.00, n=1510	0.35107
Median	30.1 (27.2, 34.3)	30.1 (27.2, 34.1)	30.2 (27.3, 34.3)	30.5 (27.2, 34.5)	

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
RANGE	15.8 , 85.1	17.4 , 85.1	18.4 , 70.2	15.8 , 70.0	
BMI < 25	10.2 % (859/8397)	10.9 % (360/3307)	9.7 % (349/3580)	9.9 % (150/1510)	0.27289
BMI: 25 - 30	37.7 % (3165/8397)	37.8 % (1249/3307)	38.0 % (1362/3580)	36.7 % (554/1510)	0.65541
BMI > 30	52.1 % (4373/8397)	51.3 % (1698/3307)	52.2 % (1869/3580)	53.4 % (806/1510)	0.41557
Waist circumference [cm]	107.65 ± 14.40, n=3229	107.06 ± 14.88, n=1286	108.05 ± 13.86, n=1463	108.00 ± 14.70, n=480	0.47229
Median	106.0 (98.0, 116.0)	106.0 (98.0, 116.0)	106.0 (98.0, 116.0)	106.0 (98.0, 116.0)	
RANGE	62.0 , 190.0	66.0 , 160.0	62.0 , 190.0	64.0 , 174.0	
Known diabetes [years]	6.90 ± 5.63, n=8312	6.00 ± 5.22, n=3270	7.34 ± 5.76, n=3544	7.82 ± 5.88, n=1498	<.00001
Participation in diabetes training	72.1 % (6054/8399)	71.3 % (2356/3306)	72.8 % (2606/3579)	72.1 % (1092/1514)	0.35850
Participation in DMP for diabetes	85.2 % (7159/8401)	85.4 % (2822/3306)	85.3 % (3053/3580)	84.8 % (1284/1515)	0.85038
Health insurance	98.1 % (8402/8567)	98.9 % (3306/3342)	98.8 % (3581/3625)	94.7 % (1515/1600)	<.00001
Statutory health insurance	96.3 % (8087/8402)	96.0 % (3175/3306)	96.0 % (3439/3581)	97.2 % (1473/1515)	0.08684
Private health insurance	3.7 % (315/8402)	4.0 % (131/3306)	4.0 % (142/3581)	2.8 % (42/1515)	0.08684
In need of care	2.6 % (219/8395)	1.7 % (57/3305)	2.5 % (91/3580)	4.7 % (71/1510)	<.00001
Level 1 of care	84.9 % (186/219)	82.5 % (47/57)	89.0 % (81/91)	81.7 % (58/71)	0.36075
Level 2 of care	13.7 % (30/219)	15.8 % (9/57)	9.9 % (9/91)	16.9 % (12/71)	0.37845
Level 3 of care	1.4 % (3/219)	1.8 % (1/57)	1.1 % (1/91)	1.4 % (1/71)	0.94525
Social status					
Employed	30.7 % (2578/8398)	35.9 % (1186/3305)	26.4 % (944/3581)	29.6 % (448/1512)	<.00001
Economically inactive	64.1 % (5386/8398)	58.9 % (1948/3305)	68.0 % (2435/3581)	66.3 % (1003/1512)	<.00001
Unemployed	13.1 % (703/5386)	13.4 % (261/1948)	13.6 % (331/2435)	11.1 % (111/1003)	0.11544
Housewife/househusband	4.9 % (262/5386)	4.9 % (96/1948)	4.3 % (104/2435)	6.2 % (62/1003)	0.05993
Retirement	81.1 % (4368/5386)	80.3 % (1565/1948)	81.4 % (1983/2435)	81.8 % (820/1003)	0.54946
Incapable of working	1.0 % (53/5386)	1.3 % (26/1948)	0.7 % (17/2435)	1.0 % (10/1003)	0.10526
Other status	0.7 % (62/8398)	0.8 % (26/3305)	0.8 % (28/3581)	0.5 % (8/1512)	0.57652
Status unknown	4.4 % (372/8398)	4.4 % (145/3305)	4.9 % (174/3581)	3.5 % (53/1512)	0.09902
Patient lives alone	20.4 % (1712/8381)	18.5 % (610/3291)	20.9 % (750/3581)	23.3 % (352/1509)	0.00040
Education					

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
1-8 years at school	31.4 % (2638/8395)	28.4 % (940/3305)	33.0 % (1181/3579)	34.2 % (517/1511)	<.00001
9-12 years at school	23.6 % (1980/8395)	23.5 % (777/3305)	23.7 % (850/3579)	23.4 % (353/1511)	0.94844
Commercial / technical school	7.8 % (654/8395)	8.4 % (276/3305)	8.0 % (286/3579)	6.1 % (92/1511)	0.02088
University	4.3 % (358/8395)	4.7 % (154/3305)	4.1 % (148/3579)	3.7 % (56/1511)	0.27747
Unknown	32.9 % (2765/8395)	35.0 % (1158/3305)	31.1 % (1114/3579)	32.6 % (493/1511)	0.00250
Smoker	11.7 % (978/8376)	11.4 % (375/3288)	11.9 % (427/3581)	11.7 % (176/1507)	0.79947
Ex-smoker	15.2 % (1274/8376)	14.6 % (479/3288)	15.4 % (552/3581)	16.1 % (243/1507)	0.34223
Non-smoker	73.1 % (6124/8376)	74.0 % (2434/3288)	72.7 % (2602/3581)	72.2 % (1088/1507)	0.29933
Alcohol consumption	61.8 % (5170/8371)	61.5 % (2020/3286)	62.5 % (2236/3580)	60.7 % (914/1505)	0.46573
Monthly	47.0 % (2429/5170)	45.8 % (925/2020)	46.9 % (1048/2236)	49.9 % (456/914)	0.11861
Weekly	40.4 % (2087/5170)	41.2 % (832/2020)	40.5 % (905/2236)	38.3 % (350/914)	0.33132
Daily	12.6 % (654/5170)	13.0 % (263/2020)	12.7 % (283/2236)	11.8 % (108/914)	0.66194
Physical exercise					
less than 1 hour/week	33.5 % (2806/8378)	31.7 % (1043/3290)	32.6 % (1167/3578)	39.5 % (596/1510)	<.00001
1 hour/week	18.1 % (1518/8378)	16.9 % (556/3290)	18.1 % (648/3578)	20.8 % (314/1510)	0.00503
2 hours/week	17.9 % (1498/8378)	17.8 % (586/3290)	18.6 % (664/3578)	16.4 % (248/1510)	0.19102
3 hours/week	13.2 % (1105/8378)	14.8 % (488/3290)	13.6 % (487/3578)	8.6 % (130/1510)	<.00001
4 hours/week	7.0 % (588/8378)	7.5 % (246/3290)	7.0 % (250/3578)	6.1 % (92/1510)	0.21769
5 hours/week	4.0 % (333/8378)	4.7 % (155/3290)	3.6 % (130/3578)	3.2 % (48/1510)	0.01596
6 hours/week	2.1 % (178/8378)	2.4 % (79/3290)	2.1 % (76/3578)	1.5 % (23/1510)	0.14682
7 hours/week	1.6 % (134/8378)	1.5 % (50/3290)	1.6 % (59/3578)	1.7 % (25/1510)	0.89638
8 hours/week	0.7 % (60/8378)	0.8 % (26/3290)	0.8 % (28/3578)	0.4 % (6/1510)	0.26787
9 or more hours/week	1.9 % (158/8378)	1.9 % (61/3290)	1.9 % (69/3578)	1.9 % (28/1510)	0.96989

Table 9-15. *Comorbid diseases in the HbA1c treatment groups at baseline.*

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
Vascular concomitant diseases	34.2 % (2928/8567)	32.1 % (1072/3342)	35.4 % (1282/3625)	35.9 % (574/1600)	0.00434
Coronary Heart Disease	23.9 % (1996/8356)	23.9 % (784/3280)	23.0 % (821/3577)	26.1 % (391/1499)	0.05786
History of myocardial infarction	8.3 % (696/8354)	7.7 % (254/3280)	8.7 % (312/3577)	8.7 % (130/1497)	0.29492
History of PCI	6.7 % (556/8351)	5.9 % (193/3279)	7.1 % (254/3575)	7.3 % (109/1497)	0.07318
History of CABG	3.6 % (299/8352)	2.8 % (93/3279)	3.9 % (140/3576)	4.4 % (66/1497)	0.00911
History of stroke/TIA	6.1 % (509/8352)	5.1 % (167/3279)	6.9 % (245/3576)	6.5 % (97/1497)	0.00778
Heart Failure	13.4 % (1119/8353)	11.5 % (378/3280)	13.6 % (485/3576)	17.1 % (256/1497)	<.00001
NYHA I	34.7 % (388/1118)	36.6 % (138/377)	35.7 % (173/485)	30.1 % (77/256)	0.20006
NYHA II	58.1 % (649/1118)	58.4 % (220/377)	56.1 % (272/485)	61.3 % (157/256)	0.38383
NYHA III	6.5 % (73/1118)	4.2 % (16/377)	7.4 % (36/485)	8.2 % (21/256)	0.08065
NYHA IV	0.7 % (8/1118)	0.8 % (3/377)	0.8 % (4/485)	0.4 % (1/256)	0.78037
Peripheral arterial occlusive disease	6.8 % (568/8352)	4.9 % (160/3280)	7.6 % (270/3575)	9.2 % (138/1497)	<.00001
Other and/or diabetes-related diseases	84.9 % (7271/8567)	82.9 % (2770/3342)	87.5 % (3172/3625)	83.1 % (1329/1600)	<.00001
Dyslipidemia	57.8 % (4828/8355)	54.7 % (1794/3280)	59.0 % (2110/3576)	61.6 % (924/1499)	<.00001
Autonomous neuropathy	12.7 % (1061/8362)	9.5 % (311/3281)	14.1 % (504/3578)	16.4 % (246/1503)	<.00001
Non-proliferative diabetic retinopathy	4.2 % (352/8371)	3.2 % (105/3295)	5.1 % (184/3576)	4.2 % (63/1500)	0.00028
Proliferative diabetic retinopathy / laser coagulation	1.1 % (90/8369)	0.7 % (23/3295)	1.2 % (44/3575)	1.5 % (23/1499)	0.01665
Diabetic macular edema	0.8 % (65/7970)	0.6 % (19/3160)	0.9 % (31/3386)	1.1 % (15/1424)	0.20110
Ophthalmologist consultation	71.1 % (5954/8370)	68.4 % (2252/3292)	73.2 % (2619/3578)	72.2 % (1083/1500)	0.00004
Blindness	0.4 % (30/8383)	0.3 % (11/3297)	0.4 % (15/3581)	0.3 % (4/1505)	0.67503
Dialysis	0.1 % (9/8385)	0.2 % (5/3297)	0.1 % (2/3582)	0.1 % (2/1506)	0.45359
History of amputation	0.5 % (47/8567)	0.5 % (18/3342)	0.4 % (15/3625)	0.9 % (14/1600)	0.11431
Foot	14.9 % (7/47)	22.2 % (4/18)	0.0 % (0/15)	21.4 % (3/14)	0.14519
Toes	57.4 % (27/47)	55.6 % (10/18)	66.7 % (10/15)	50.0 % (7/14)	0.64871
Lower extremities	25.5 % (12/47)	33.3 % (6/18)	20.0 % (3/15)	21.4 % (3/14)	0.62450

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
Upper extremities	6.4 % (3/47)	0.0 % (0/18)	13.3 % (2/15)	7.1 % (1/14)	0.29325
Other concomitant diseases	46.1 % (3856/8368)	43.1 % (1414/3283)	47.2 % (1687/3577)	50.1 % (755/1508)	<.00001

Table 9-16.*Available laboratory values at baseline (last six weeks) in the HbA1c treatment groups.*

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
No. of patients	8567 (100.0 %)	3342 (39.0 %)	3625 (42.3 %)	1600 (18.7 %)	
Total fasting cholesterol available	82.9 % (7099/8567)	84.1 % (2811/3342)	83.1 % (3012/3625)	79.8 % (1276/1600)	0.00064
Total fasting cholesterol [mmol/L]	5.31 ± 1.21, n=7099	5.32 ± 1.15, n=2811	5.29 ± 1.24, n=3012	5.36 ± 1.28, n=1276	0.09041
Fasting HDL-cholesterol available	70.4 % (6032/8567)	70.8 % (2366/3342)	70.8 % (2567/3625)	68.7 % (1099/1600)	0.24646
Fasting HDL-cholesterol [mmol/L]	1.26 ± 0.40, n=6032	1.30 ± 0.40, n=2366	1.25 ± 0.38, n=2567	1.23 ± 0.42, n=1099	<.00001
Fasting LDL-cholesterol available	69.9 % (5987/8567)	70.6 % (2359/3342)	70.0 % (2539/3625)	68.1 % (1089/1600)	0.18744
Fasting LDL-cholesterol [mmol/L]	3.20 ± 1.01, n=5987	3.20 ± 1.00, n=2359	3.20 ± 1.00, n=2539	3.22 ± 1.06, n=1089	0.90305
Fasting triglycerides available	74.0 % (6340/8567)	75.1 % (2510/3342)	74.5 % (2699/3625)	70.7 % (1131/1600)	0.00297
Fasting triglycerides [mmol/L]	2.32 ± 1.64, n=6340	2.21 ± 1.48, n=2510	2.31 ± 1.61, n=2699	2.57 ± 1.96, n=1131	<.00001
Fasting glucose available	83.1 % (7119/8567)	84.8 % (2835/3342)	84.5 % (3062/3625)	76.4 % (1222/1600)	<.00001
Fasting glucose [mmol/L]	8.51 ± 2.78, n=7119	7.75 ± 2.56, n=2835	8.74 ± 2.61, n=3062	9.71 ± 3.14, n=1222	<.00001
Postprandial glucose available	48.8 % (4178/8567)	47.5 % (1586/3342)	51.9 % (1880/3625)	44.5 % (712/1600)	<.00001
Postprandial glucose [mmol/L]	10.87 ± 3.40, n=4178	9.97 ± 3.17, n=1586	11.15 ± 3.27, n=1880	12.11 ± 3.68, n=712	<.00001
Hb1Ac available	94.5 % (8099/8567)	95.4 % (3188/3342)	95.3 % (3456/3625)	90.9 % (1455/1600)	<.00001
HbA1c [%]	7.80 ± 2.13, n=8099	7.25 ± 1.26, n=3188	7.96 ± 2.76, n=3456	8.63 ± 1.48, n=1455	<.00001
Haemoglobin available	60.2 % (5161/8567)	58.4 % (1952/3342)	62.5 % (2265/3625)	59.0 % (944/1600)	0.00128
Haemoglobin [mmol/L]	8.26 ± 1.45, n=5161	8.17 ± 1.50, n=1952	8.29 ± 1.46, n=2265	8.38 ± 1.33, n=944	0.01354
Serum creatinine available	82.5 % (7067/8567)	83.4 % (2788/3342)	82.8 % (3003/3625)	79.8 % (1276/1600)	0.00489
Serum creatinine [µmol/l]	85.53 ± 56.93, n=7067	86.26 ± 68.53, n=2788	84.90 ± 43.24, n=3003	85.40 ± 57.36, n=1276	0.05639
eGFR according to MDRD formula [ml/min]	81.81 ± 24.52, n=7067	82.71 ± 24.95, n=2788	80.97 ± 23.62, n=3003	81.80 ± 25.57, n=1276	0.01253
Microalbustix albumin [mg/l]	32.25 ± 37.50, n=1549	29.91 ± 35.15, n=562	34.16 ± 38.25, n=731	31.90 ± 40.11, n=256	0.03713
Microalbustix creatinine [mg/dl]	56.83 ± 77.41, n=799	59.50 ± 77.19, n=293	58.25 ± 78.70, n=370	47.18 ± 74.09, n=136	0.09745

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
Macroalbuminuria: positive test	10.5 % (588/5615)	9.7 % (208/2142)	9.9 % (246/2476)	13.4 % (134/997)	0.00326
Macroalbuminuria: negative test	89.5 % (5027/5615)	90.3 % (1934/2142)	90.1 % (2230/2476)	86.6 % (863/997)	0.00326
Increased liver function readings	19.6 % (1237/6304)	18.4 % (461/2507)	19.1 % (509/2665)	23.6 % (267/1132)	0.00084

Table 9-17. *Previous antidiabetic therapy in the HbA1c treatment groups before baseline.*

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
No. of patients	8567 (100.0 %)	3342 (39.0 %)	3625 (42.3 %)	1600 (18.7 %)	
Metformin	79.9 % (6686/8373)	77.8 % (2562/3294)	81.5 % (2912/3575)	80.6 % (1212/1504)	0.00055
Metformin, dosage [mg/day]	1618.04 ± 582.18, n=6666	1535.44 ± 594.55, n=2546	1679.84 ± 566.77, n=2911	1643.19 ± 572.05, n=1209	<.00001
Duration of metformin treatment [yrs]	3.2 (1.4, 6.1)	2.7 (1.2, 5.1)	3.5 (1.6, 6.7)	3.6 (1.4, 6.9)	<.00001
Sulfonylurea drugs	23.9 % (1999/8362)	18.6 % (611/3291)	26.0 % (930/3571)	30.5 % (458/1500)	<.00001
Sulfonylurea drugs, dosage [mg/day]	3.40 ± 1.91, n=1998	3.19 ± 1.86, n=610	3.45 ± 1.91, n=930	3.57 ± 1.93, n=458	0.00155
Duration of sulfonylurea treatment [yrs]	3.5 (1.6, 6.3)	3.0 (1.3, 5.5)	3.7 (1.8, 6.6)	3.7 (1.6, 6.7)	0.00003
Substance					
Carbutamide	0.0 % (0/1999)	0.0 % (0/611)	0.0 % (0/930)	0.0 % (0/458)	
Tolbutamide	0.0 % (0/1999)	0.0 % (0/611)	0.0 % (0/930)	0.0 % (0/458)	
Glibenclamide	25.5 % (509/1999)	26.5 % (162/611)	24.8 % (231/930)	25.3 % (116/458)	0.75921
Glibornuride	0.0 % (0/1999)	0.0 % (0/611)	0.0 % (0/930)	0.0 % (0/458)	
Gliclazide	0.1 % (1/1999)	0.2 % (1/611)	0.0 % (0/930)	0.0 % (0/458)	0.32097
Glipizide	0.0 % (0/1999)	0.0 % (0/611)	0.0 % (0/930)	0.0 % (0/458)	
Gliquidone	0.4 % (7/1999)	0.2 % (1/611)	0.4 % (4/930)	0.4 % (2/458)	0.64481
Glisoxepide	0.0 % (0/1999)	0.0 % (0/611)	0.0 % (0/930)	0.0 % (0/458)	
Glycodiazine	0.3 % (5/1999)	0.8 % (5/611)	0.0 % (0/930)	0.0 % (0/458)	0.00337
Glimepiride	73.2 % (1463/1999)	71.7 % (438/611)	74.1 % (689/930)	73.4 % (336/458)	0.57928
Other	0.7 % (14/1999)	0.7 % (4/611)	0.6 % (6/930)	0.9 % (4/458)	0.87977
Glucosidase inhibitors	2.4 % (197/8361)	2.3 % (75/3289)	2.7 % (97/3570)	1.7 % (25/1502)	0.07327
Glucosidase inhibitors, dosage [mg/day]	146.57 ± 86.34, n=197	138.17 ± 89.38, n=75	155.15 ± 80.52, n=97	138.44 ± 98.62, n=25	0.11733
Duration of treatment with glucosidase inhibitors [yrs]	2.7 (1.1, 6.1)	2.5 (1.1, 5.6)	2.9 (1.0, 7.1)	2.8 (1.4, 5.3)	0.82815
Substance					
Acarbose	92.4 % (182/197)	93.3 % (70/75)	93.8 % (91/97)	84.0 % (21/25)	0.23736
Miglitol	5.6 % (11/197)	4.0 % (3/75)	5.2 % (5/97)	12.0 % (3/25)	0.30991
Other	2.0 % (4/197)	2.7 % (2/75)	1.0 % (1/97)	4.0 % (1/25)	0.56913

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
Glinide	3.2 % (265/8356)	2.5 % (82/3283)	3.4 % (122/3572)	4.1 % (61/1501)	0.00892
Glinide, dosage [mg/day]	23.73 ± 73.24, n=265	28.06 ± 80.05, n=82	20.52 ± 70.09, n=122	24.33 ± 70.71, n=61	0.08941
Duration of glinide treatment [yrs]	2.6 (1.1, 5.5)	2.3 (1.1, 5.3)	3.2 (1.2, 5.5)	2.7 (1.0, 6.4)	0.62337
Substance					
Nateglinide	7.9 % (21/265)	12.2 % (10/82)	6.6 % (8/122)	4.9 % (3/61)	0.21037
Repaglinide	86.4 % (229/265)	82.9 % (68/82)	88.5 % (108/122)	86.9 % (53/61)	0.51585
Other	5.7 % (15/265)	4.9 % (4/82)	4.9 % (6/122)	8.2 % (5/61)	0.62041
Glitazone	1.4 % (121/8362)	1.4 % (46/3289)	1.6 % (57/3571)	1.2 % (18/1502)	0.53198
Glitazone, dosage [mg/day]	30.81 ± 12.45, n=120	31.67 ± 11.26, n=46	31.68 ± 12.22, n=57	25.53 ± 15.43, n=17	0.42604
Duration of glitazone treatment [yrs]	3.8 (2.4, 5.4)	3.4 (1.8, 5.2)	3.9 (2.8, 5.2)	5.1 (2.9, 7.3)	0.23271
Substance					
Pioglitazon	87.5 % (105/120)	91.3 % (42/46)	87.7 % (50/57)	76.5 % (13/17)	0.28622
Other	12.5 % (15/120)	8.7 % (4/46)	12.3 % (7/57)	23.5 % (4/17)	0.28622
DPP-4 inhibitors	17.7 % (1482/8353)	15.6 % (510/3279)	18.7 % (668/3572)	20.2 % (304/1502)	0.00006
DPP-4 inhibitors, dosage [mg/day]	84.65 ± 35.18, n=1481	83.58 ± 36.30, n=510	85.65 ± 31.76, n=668	84.26 ± 40.15, n=303	0.20927
Duration of DPP-4 inhibitor treatment [yrs]	1.4 (0.6, 2.4)	1.4 (0.6, 2.3)	1.4 (0.6, 2.4)	1.5 (0.6, 2.7)	0.55349
Substance					
Sitagliptin	49.1 % (727/1481)	46.3 % (236/510)	49.9 % (333/668)	52.1 % (158/303)	0.23412
Vildagliptin	44.6 % (660/1481)	47.1 % (240/510)	44.2 % (295/668)	41.3 % (125/303)	0.26285
Linagliptin	0.0 % (0/1481)	0.0 % (0/510)	0.0 % (0/668)	0.0 % (0/303)	
Saxagliptin	5.8 % (86/1481)	6.1 % (31/510)	5.4 % (36/668)	6.3 % (19/303)	0.81835
Other	0.5 % (8/1481)	0.6 % (3/510)	0.6 % (4/668)	0.3 % (1/303)	0.85483
SGTL-2 inhibitors	0.2 % (16/8354)	0.1 % (4/3281)	0.3 % (9/3571)	0.2 % (3/1502)	0.46746
SGTL-2 inhibitors, dosage [mg/day]	17.56 ± 24.26, n=16	9.00 ± 2.00, n=4	24.44 ± 31.27, n=9	8.33 ± 2.89, n=3	0.14298
Duration of SGTL-2 inhibitor treatment [yrs]	0.3 (0.2, 0.8)	0.3 (0.2, 0.7)	0.3 (0.2, 0.4)	2.5 (0.1, 3.9)	0.67684
Substance					
Dapagliflozin	68.8 % (11/16)	75.0 % (3/4)	66.7 % (6/9)	66.7 % (2/3)	0.95267

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
Other	31.3 % (5/16)	25.0 % (1/4)	33.3 % (3/9)	33.3 % (1/3)	0.95267
Fixed-dose combination metformin / DPP-4 inhibitor	77.5 % (914/1179)	74.9 % (295/394)	77.3 % (415/537)	82.3 % (204/248)	0.09086
Novartis drugs					
Vildagliptin / Metformin					
Eucreas	85.7 % (396/462)	86.3 % (138/160)	86.1 % (179/208)	84.0 % (79/94)	0.87281
Icandra	14.3 % (66/462)	13.8 % (22/160)	13.9 % (29/208)	16.0 % (15/94)	0.87281
Vildagliptin					
Galvus	68.2 % (135/198)	63.8 % (51/80)	70.1 % (61/87)	74.2 % (23/31)	0.49893
Jalra	31.8 % (63/198)	36.3 % (29/80)	29.9 % (26/87)	25.8 % (8/31)	0.49893
Nateglinide					
STARLIX	95.2 % (20/21)	100.0 % (10/10)	87.5 % (7/8)	100.0 % (3/3)	0.42608
Other	4.8 % (1/21)	0.0 % (0/10)	12.5 % (1/8)	0.0 % (0/3)	0.42608

Table 9-18. *Reasons for pharmacotherapy change in the HbA1c treatment groups at baseline.*

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
No. of patients	8567 (100.0 %)	3342 (39.0 %)	3625 (42.3 %)	1600 (18.7 %)	
Blood glucose adjustment	87.8 % (7329/8345)	84.9 % (2775/3270)	89.3 % (3192/3574)	90.7 % (1362/1501)	<.00001
Weight gain	19.8 % (1652/8345)	21.3 % (695/3270)	20.5 % (733/3574)	14.9 % (224/1501)	<.00001
Hypoglycemia	3.8 % (321/8345)	3.1 % (102/3270)	4.1 % (145/3574)	4.9 % (74/1501)	0.00719
Other reasons	19.0 % (1584/8345)	21.7 % (708/3270)	17.7 % (634/3574)	16.1 % (242/1501)	<.00001

Table 9-19. *Current antidiabetic therapy in the HbA1c treatment groups at baseline.*

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
No. of patients	8567 (100.0 %)	3342 (39.0 %)	3625 (42.3 %)	1600 (18.7 %)	
Metformin	80.0 % (6682/8355)	78.8 % (2584/3281)	81.0 % (2894/3572)	80.2 % (1204/1502)	0.06376
Metformin, dosage [mg/day]	1711.80 ± 540.55, n=6664	1629.21 ± 559.81, n=2572	1772.63 ± 512.90, n=2890	1742.26 ± 541.23, n=1202	<.00001
Sulfonylurea drugs	17.5 % (1462/8351)	15.2 % (500/3282)	18.0 % (643/3570)	21.3 % (319/1499)	<.00001
Sulfonylurea drugs, dosage [mg/day]	3.21 ± 1.90, n=1461	3.05 ± 1.86, n=499	3.27 ± 1.89, n=643	3.33 ± 1.97, n=319	0.02381
Substance					
Carbutamide	0.0 % (0/1461)	0.0 % (0/499)	0.0 % (0/643)	0.0 % (0/319)	
Tolbutamide	0.0 % (0/1461)	0.0 % (0/499)	0.0 % (0/643)	0.0 % (0/319)	
Glibenclamide	21.4 % (313/1461)	25.9 % (129/499)	19.0 % (122/643)	19.4 % (62/319)	0.01195
Glibornuride	0.0 % (0/1461)	0.0 % (0/499)	0.0 % (0/643)	0.0 % (0/319)	
Gliclazide	0.1 % (1/1461)	0.2 % (1/499)	0.0 % (0/643)	0.0 % (0/319)	0.38114
Glipizide	0.0 % (0/1461)	0.0 % (0/499)	0.0 % (0/643)	0.0 % (0/319)	
Gliquidone	0.3 % (5/1461)	0.2 % (1/499)	0.5 % (3/643)	0.3 % (1/319)	0.74324
Glisoxepide	0.1 % (2/1461)	0.4 % (2/499)	0.0 % (0/643)	0.0 % (0/319)	0.14508
Glycodiazine	1.2 % (18/1461)	1.6 % (8/499)	1.2 % (8/643)	0.6 % (2/319)	0.46638
Glimepiride	76.3 % (1115/1461)	71.3 % (356/499)	78.7 % (506/643)	79.3 % (253/319)	0.00546
Other	0.5 % (7/1461)	0.4 % (2/499)	0.6 % (4/643)	0.3 % (1/319)	0.76976
Glucosidase inhibitors	1.1 % (91/8354)	1.0 % (33/3284)	1.3 % (46/3571)	0.8 % (12/1499)	0.26080
Glucosidase inhibitors, dosage [mg/day]	151.62 ± 88.79, n=90	109.91 ± 43.51, n=32	173.04 ± 90.08, n=46	180.76 ± 131.69, n=12	0.00757
Substance					
Acarbose	91.1 % (82/90)	84.4 % (27/32)	93.5 % (43/46)	100.0 % (12/12)	0.19380
Miglitol	7.8 % (7/90)	15.6 % (5/32)	4.3 % (2/46)	0.0 % (0/12)	0.10468
Other	1.1 % (1/90)	0.0 % (0/32)	2.2 % (1/46)	0.0 % (0/12)	0.61654
Glinide	3.5 % (290/8342)	2.2 % (73/3272)	3.8 % (135/3571)	5.5 % (82/1499)	<.00001
Glinide, dosage [mg/day]	14.38 ± 56.32, n=290	15.26 ± 59.70, n=73	13.42 ± 54.03, n=135	15.16 ± 57.59, n=82	0.98567
Substance					
Nateglinide	2.8 % (8/290)	2.7 % (2/73)	3.0 % (4/135)	2.4 % (2/82)	0.97417
Repaglinide	94.1 % (273/290)	95.9 % (70/73)	91.9 % (124/135)	96.3 % (79/82)	0.30025
Other	3.1 % (9/290)	1.4 % (1/73)	5.2 % (7/135)	1.2 % (1/82)	0.16179

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
Glitazone	0.5 % (43/8352)	0.4 % (14/3284)	0.7 % (24/3569)	0.3 % (5/1499)	0.20236
Glitazone, dosage [mg/day]	38.00 ± 22.38, n=42	33.57 ± 12.47, n=14	42.50 ± 26.17, n=24	26.50 ± 22.11, n=4	0.46025
Substance					
Pioglitazon	88.1 % (37/42)	100.0 % (14/14)	79.2 % (19/24)	100.0 % (4/4)	0.11903
Other	11.9 % (5/42)	0.0 % (0/14)	20.8 % (5/24)	0.0 % (0/4)	0.11903
DPP-4 inhibitors	62.5 % (5212/8342)	59.3 % (1940/3270)	65.3 % (2331/3572)	62.7 % (941/1500)	<.00001
DPP-4 inhibitors, dosage [mg/day]	84.81 ± 33.04, n=5209	84.33 ± 31.92, n=1939	85.18 ± 34.42, n=2330	84.87 ± 31.82, n=940	0.09389
Substance					
Sitagliptin	28.4 % (1481/5211)	28.1 % (544/1939)	28.0 % (652/2331)	30.3 % (285/941)	0.37346
Vildagliptin	66.9 % (3487/5211)	68.0 % (1318/1939)	67.0 % (1561/2331)	64.6 % (608/941)	0.19812
Linagliptin	0.0 % (1/5211)	0.1 % (1/1939)	0.0 % (0/2331)	0.0 % (0/941)	0.43003
Saxagliptin	4.3 % (222/5211)	3.6 % (69/1939)	4.7 % (110/2331)	4.6 % (43/941)	0.15225
Other	0.4 % (20/5211)	0.4 % (7/1939)	0.3 % (8/2331)	0.5 % (5/941)	0.71797
GLP-1 analogs/mimetics	4.8 % (404/8357)	4.2 % (139/3286)	5.4 % (193/3571)	4.8 % (72/1500)	0.07667
GLP-1 analogs/mimetics, dosage [mg/day]	6.27 ± 12.93, n=401	6.16 ± 11.85, n=139	6.64 ± 13.93, n=191	5.48 ± 12.25, n=71	0.74040
Substance					
Exenatide	43.9 % (177/403)	45.3 % (63/139)	42.7 % (82/192)	44.4 % (32/72)	0.88972
Liraglutide	50.4 % (203/403)	45.3 % (63/139)	54.2 % (104/192)	50.0 % (36/72)	0.28267
Other	5.7 % (23/403)	9.4 % (13/139)	3.1 % (6/192)	5.6 % (4/72)	0.05463
SGTL-2 inhibitors	1.8 % (147/8358)	1.7 % (55/3287)	1.7 % (60/3571)	2.1 % (32/1500)	0.47601
SGTL-2 inhibitors, dosage [mg/day]	13.63 ± 16.38, n=145	14.45 ± 18.45, n=55	14.34 ± 17.77, n=59	10.81 ± 7.43, n=31	0.27994
Substance					
Dapagliflozin	95.2 % (138/145)	94.5 % (52/55)	93.2 % (55/59)	100.0 % (31/31)	0.34839
Other	4.8 % (7/145)	5.5 % (3/55)	6.8 % (4/59)	0.0 % (0/31)	0.34839
Total number of oral antidiabetics	1.71 ± 0.70, n=8363	1.62 ± 0.68, n=3289	1.77 ± 0.68, n=3572	1.78 ± 0.76, n=1502	<.00001
Median	2.0 (1.0, 2.0)	2.0 (1.0, 2.0)	2.0 (1.0, 2.0)	2.0 (1.0, 2.0)	
RANGE	0.0 , 5.0	0.0 , 5.0	0.0 , 4.0	0.0 , 4.0	
None	3.9 % (328/8363)	4.3 % (143/3289)	2.8 % (99/3572)	5.7 % (86/1502)	<.00001
1 OAD	30.6 % (2555/8363)	35.7 % (1173/3289)	28.3 % (1011/3572)	24.7 % (371/1502)	<.00001

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
2 OADs	56.1 % (4689/8363)	53.5 % (1758/3289)	58.3 % (2081/3572)	56.6 % (850/1502)	0.00029
>= 3 OADs	9.5 % (791/8363)	6.5 % (215/3289)	10.7 % (381/3572)	13.0 % (195/1502)	<.00001
Insulin(rapid-acting or long-acting or Pre-mixed)	15.1 % (1290/8567)	9.8 % (329/3342)	17.4 % (631/3625)	20.6 % (330/1600)	<.00001
Rapid-acting insulin	4.3 % (357/8360)	3.6 % (118/3286)	4.1 % (146/3576)	6.2 % (93/1498)	0.00014
Human insulin	50.1 % (179/357)	51.7 % (61/118)	45.9 % (67/146)	54.8 % (51/93)	0.36971
Analogues	49.9 % (178/357)	48.3 % (57/118)	54.1 % (79/146)	45.2 % (42/93)	0.36971
Syringe	3.4 % (12/357)	1.7 % (2/118)	3.4 % (5/146)	5.4 % (5/93)	0.33739
Pen	96.6 % (345/357)	98.3 % (116/118)	96.6 % (141/146)	94.6 % (88/93)	0.33739
Pump	0.0 % (0/357)	0.0 % (0/118)	0.0 % (0/146)	0.0 % (0/93)	
Other	0.0 % (0/357)	0.0 % (0/118)	0.0 % (0/146)	0.0 % (0/93)	
U-40	22.5 % (80/355)	27.1 % (32/118)	17.9 % (26/145)	23.9 % (22/92)	0.19390
U-100	77.5 % (275/355)	72.9 % (86/118)	82.1 % (119/145)	76.1 % (70/92)	0.19390
1x insulin/day	8.1 % (29/357)	11.0 % (13/118)	5.5 % (8/146)	8.6 % (8/93)	0.25669
2x insulin/day	16.0 % (57/357)	20.3 % (24/118)	10.3 % (15/146)	19.4 % (18/93)	0.04970
3x insulin/day	74.2 % (265/357)	67.8 % (80/118)	82.9 % (121/146)	68.8 % (64/93)	0.00789
4x insulin/day	1.7 % (6/357)	0.8 % (1/118)	1.4 % (2/146)	3.2 % (3/93)	0.38198
Long-acting insulin	12.6 % (1056/8361)	8.4 % (275/3286)	14.7 % (527/3575)	16.9 % (254/1500)	<.00001
Human insulin	30.0 % (317/1056)	33.5 % (92/275)	25.6 % (135/527)	35.4 % (90/254)	0.00691
Analogues	70.0 % (739/1056)	66.5 % (183/275)	74.4 % (392/527)	64.6 % (164/254)	0.00691
Syringe	5.8 % (61/1056)	4.0 % (11/275)	6.1 % (32/527)	7.1 % (18/254)	0.28936
Pen	93.8 % (991/1056)	96.0 % (264/275)	93.4 % (492/527)	92.5 % (235/254)	0.20199
Pump	0.2 % (2/1056)	0.0 % (0/275)	0.4 % (2/527)	0.0 % (0/254)	0.36579
Other	0.2 % (2/1056)	0.0 % (0/275)	0.2 % (1/527)	0.4 % (1/254)	0.58197
U-40	16.3 % (171/1049)	17.5 % (48/275)	12.8 % (67/523)	22.3 % (56/251)	0.00305

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
U-100	83.7 % (878/1049)	82.5 % (227/275)	87.2 % (456/523)	77.7 % (195/251)	0.00305
1x insulin/day	88.1 % (930/1056)	84.7 % (233/275)	90.3 % (476/527)	87.0 % (221/254)	0.05665
2x insulin/day	10.1 % (107/1056)	11.3 % (31/275)	9.1 % (48/527)	11.0 % (28/254)	0.54297
3x insulin/day	1.6 % (17/1056)	3.6 % (10/275)	0.6 % (3/527)	1.6 % (4/254)	0.00467
4x insulin/day	0.2 % (2/1056)	0.4 % (1/275)	0.0 % (0/527)	0.4 % (1/254)	0.36741
Pre-mixed insulin	1.6 % (133/8360)	0.6 % (21/3286)	2.0 % (70/3574)	2.8 % (42/1500)	<.00001
Human insulin	56.4 % (75/133)	57.1 % (12/21)	61.4 % (43/70)	47.6 % (20/42)	0.36035
Analogues	43.6 % (58/133)	42.9 % (9/21)	38.6 % (27/70)	52.4 % (22/42)	0.36035
Syringe	4.5 % (6/133)	0.0 % (0/21)	2.9 % (2/70)	9.5 % (4/42)	0.14324
Pen	95.5 % (127/133)	100.0 % (21/21)	97.1 % (68/70)	90.5 % (38/42)	0.14324
Pump	0.0 % (0/133)	0.0 % (0/21)	0.0 % (0/70)	0.0 % (0/42)	
Other	0.0 % (0/133)	0.0 % (0/21)	0.0 % (0/70)	0.0 % (0/42)	
U-40	18.0 % (24/133)	33.3 % (7/21)	14.3 % (10/70)	16.7 % (7/42)	0.13253
U-100	82.0 % (109/133)	66.7 % (14/21)	85.7 % (60/70)	83.3 % (35/42)	0.13253
1x insulin/day	11.3 % (15/133)	14.3 % (3/21)	7.1 % (5/70)	16.7 % (7/42)	0.27187
2x insulin/day	83.5 % (111/133)	81.0 % (17/21)	90.0 % (63/70)	73.8 % (31/42)	0.07817
3x insulin/day	3.8 % (5/133)	4.8 % (1/21)	1.4 % (1/70)	7.1 % (3/42)	0.29548
4x insulin/day	1.5 % (2/133)	0.0 % (0/21)	1.4 % (1/70)	2.4 % (1/42)	0.76282
Fixed-dose combination metformin / DPP-4 inhibitor	73.6 % (3100/4210)	74.1 % (1129/1523)	72.1 % (1371/1901)	76.3 % (600/786)	0.06744
Novartis drugs					
Vildagliptin / Metformin					
Eucreas	91.9 % (2056/2236)	92.5 % (750/811)	91.5 % (921/1007)	92.1 % (385/418)	0.72380
Icandra	8.1 % (180/2236)	7.5 % (61/811)	8.5 % (86/1007)	7.9 % (33/418)	0.72380
Vildagliptin					
Galvus	86.8 % (1086/1251)	84.0 % (426/507)	89.5 % (496/554)	86.3 % (164/190)	0.02931
Jalra	13.2 % (165/1251)	16.0 % (81/507)	10.5 % (58/554)	13.7 % (26/190)	0.02931
Nateglinide					

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
STARLIX	100.0 % (8/8)	100.0 % (2/2)	100.0 % (4/4)	100.0 % (2/2)	
Other	0.0 % (0/8)	0.0 % (0/2)	0.0 % (0/4)	0.0 % (0/2)	

Table 9-20. *Current antihypertensive therapy in the HbA1c treatment groups at baseline.*

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
No. of patients	8567 (100.0 %)	3342 (39.0 %)	3625 (42.3 %)	1600 (18.7 %)	
ACE inhibitors	52.4 % (4377/8351)	51.5 % (1693/3285)	53.7 % (1917/3572)	51.3 % (767/1494)	0.13842
ACE inhibitors, dosage [mg/day]	10.49 ± 12.67, n=4365	10.32 ± 12.55, n=1681	10.37 ± 12.08, n=1917	11.18 ± 14.25, n=767	0.00374
Substance					
Captopril	2.7 % (116/4372)	3.0 % (51/1688)	2.5 % (47/1917)	2.3 % (18/767)	0.48055
Enalapril	17.7 % (773/4372)	18.2 % (307/1688)	16.9 % (324/1917)	18.5 % (142/767)	0.48117
Lisinopril	11.4 % (500/4372)	11.1 % (188/1688)	11.7 % (225/1917)	11.3 % (87/767)	0.84929
Ramipril	65.4 % (2858/4372)	65.0 % (1098/1688)	66.1 % (1267/1917)	64.3 % (493/767)	0.62961
Trandolapril	0.1 % (6/4372)	0.1 % (2/1688)	0.1 % (2/1917)	0.3 % (2/767)	0.59195
Other	2.7 % (119/4372)	2.5 % (42/1688)	2.7 % (52/1917)	3.3 % (25/767)	0.55266
Angiotensin receptor blocker (ARB)	27.3 % (2281/8345)	27.1 % (889/3279)	28.1 % (1005/3572)	25.9 % (387/1494)	0.24962
ARB, dosage [mg/day]	115.32 ± 115.86, n=2278	120.59 ± 119.73, n=886	109.69 ± 111.10, n=1005	117.88 ± 118.60, n=387	0.16170
Substance					
Candesartan	22.9 % (522/2281)	21.3 % (189/889)	23.2 % (233/1005)	25.8 % (100/387)	0.19243
Irbesartan	5.7 % (130/2281)	6.3 % (56/889)	5.1 % (51/1005)	5.9 % (23/387)	0.50464
Losartan	7.9 % (181/2281)	8.0 % (71/889)	7.8 % (78/1005)	8.3 % (32/387)	0.94943
Valsartan	39.1 % (891/2281)	39.5 % (351/889)	39.4 % (396/1005)	37.2 % (144/387)	0.71419
Other	24.4 % (557/2281)	25.0 % (222/889)	24.6 % (247/1005)	22.7 % (88/387)	0.68638
Direct renin inhibitor	0.5 % (39/8343)	0.5 % (18/3277)	0.4 % (14/3572)	0.5 % (7/1494)	0.63462
Direct renin inhibitor, dosage [mg/day]	208.15 ± 93.96, n=39	192.56 ± 84.14, n=18	257.14 ± 70.32, n=14	150.29 ± 122.07, n=7	0.03725
Beta-blocker	46.5 % (3883/8351)	45.9 % (1507/3285)	46.5 % (1660/3572)	47.9 % (716/1494)	0.41977
Beta-blocker, dosage [mg/day]	53.25 ± 61.46, n=3873	51.66 ± 60.53, n=1497	56.91 ± 62.84, n=1660	48.08 ± 59.69, n=716	0.00047
Substance					
Metoprolol	45.2 % (1754/3881)	44.7 % (673/1505)	47.7 % (792/1660)	40.4 % (289/716)	0.00383
Bisoprolol	40.3 % (1563/3881)	41.6 % (626/1505)	38.3 % (635/1660)	42.2 % (302/716)	0.08250
Nebivolol	6.1 % (237/3881)	6.0 % (90/1505)	5.2 % (87/1660)	8.4 % (60/716)	0.01314

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
Carvedilol	4.7 % (182/3881)	4.1 % (61/1505)	5.2 % (87/1660)	4.7 % (34/716)	0.28671
Other	3.7 % (145/3881)	3.7 % (55/1505)	3.6 % (59/1660)	4.3 % (31/716)	0.64345
Calcium channel blocker	27.1 % (2257/8342)	25.6 % (838/3277)	27.6 % (985/3572)	29.1 % (434/1493)	0.02719
Calcium channel blocker, dosage [mg/day]	17.50 ± 41.24, n=2252	14.64 ± 33.35, n=834	19.15 ± 45.52, n=984	19.27 ± 44.42, n=434	0.47086
Substance					
Amlodipine	75.2 % (1697/2256)	74.5 % (624/838)	76.3 % (752/985)	74.1 % (321/433)	0.54862
Nifedipine	2.7 % (60/2256)	2.5 % (21/838)	2.3 % (23/985)	3.7 % (16/433)	0.32129
Nisoldipine	0.0 % (1/2256)	0.0 % (0/838)	0.1 % (1/985)	0.0 % (0/433)	0.52442
Nimodipine	0.0 % (1/2256)	0.1 % (1/838)	0.0 % (0/985)	0.0 % (0/433)	0.42894
Diltiazem	0.6 % (13/2256)	0.2 % (2/838)	0.6 % (6/985)	1.2 % (5/433)	0.12156
Verapamil	3.2 % (73/2256)	2.4 % (20/838)	3.4 % (33/985)	4.6 % (20/433)	0.09943
Gallopamil	0.0 % (0/2256)	0.0 % (0/838)	0.0 % (0/985)	0.0 % (0/433)	
Felodipine	2.9 % (65/2256)	2.4 % (20/838)	3.2 % (32/985)	3.0 % (13/433)	0.54045
Nitrendipine	4.3 % (97/2256)	4.7 % (39/838)	4.7 % (46/985)	2.8 % (12/433)	0.21851
Lercanidipine	9.8 % (222/2256)	12.3 % (103/838)	7.9 % (78/985)	9.5 % (41/433)	0.00730
Nilvadipine	0.0 % (1/2256)	0.0 % (0/838)	0.1 % (1/985)	0.0 % (0/433)	0.52442
Manidipine	0.0 % (1/2256)	0.1 % (1/838)	0.0 % (0/985)	0.0 % (0/433)	0.42894
Isradipine	0.1 % (3/2256)	0.2 % (2/838)	0.1 % (1/985)	0.0 % (0/433)	0.50795
Other	1.0 % (22/2256)	0.6 % (5/838)	1.2 % (12/985)	1.2 % (5/433)	0.36959
Diuretic drugs	42.6 % (3556/8348)	40.6 % (1333/3282)	43.3 % (1548/3572)	45.2 % (675/1494)	0.00625
Diuretic drugs, dosage [mg/day]	18.8 (12.5, 25.0)	18.8 (12.5, 25.0)	20.0 (12.5, 25.0)	12.5 (12.5, 25.0)	0.55537
Substance					
Furosemide	8.4 % (298/3556)	6.9 % (92/1333)	9.0 % (140/1548)	9.8 % (66/675)	0.04075
Torasemide	22.8 % (810/3556)	21.2 % (282/1333)	22.9 % (354/1548)	25.8 % (174/675)	0.06536
Bumetanide	0.0 % (1/3556)	0.0 % (0/1333)	0.1 % (1/1548)	0.0 % (0/675)	0.52269
Etacrynic acid	0.0 % (1/3556)	0.0 % (0/1333)	0.1 % (1/1548)	0.0 % (0/675)	0.52269
Piretanide	1.1 % (40/3556)	1.3 % (17/1333)	1.0 % (15/1548)	1.2 % (8/675)	0.72922
Hydrochlorothiazide	69.0 % (2452/3556)	71.8 % (957/1333)	68.4 % (1059/1548)	64.6 % (436/675)	0.00364
Clopamid	0.2 % (8/3556)	0.2 % (2/1333)	0.2 % (3/1548)	0.4 % (3/675)	0.39674
Other	8.2 % (293/3556)	7.4 % (99/1333)	8.6 % (133/1548)	9.0 % (61/675)	0.37043
Other anti-hypertensive therapy	10.2 % (849/8331)	9.1 % (298/3266)	10.8 % (386/3571)	11.0 % (165/1494)	0.03439

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
Total number of antihyper. Drugs	2.06 ± 1.15, n=8352	2.00 ± 1.15, n=3286	2.10 ± 1.14, n=3572	2.11 ± 1.18, n=1494	0.00025
Median	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)	
RANGE	0.0 , 6.0	0.0 , 6.0	0.0 , 6.0	0.0 , 6.0	
N	8352[N]	3286[N]	3572[N]	1494[N]	
None	6.5 % (542/8352)	7.2 % (236/3286)	5.5 % (197/3572)	7.3 % (109/1494)	0.00750
1 AHD	28.9 % (2411/8352)	30.7 % (1008/3286)	28.4 % (1015/3572)	26.0 % (388/1494)	0.00289
2 AHDs	29.5 % (2460/8352)	28.8 % (948/3286)	29.6 % (1059/3572)	30.3 % (453/1494)	0.55361
3 AHDs	23.9 % (1998/8352)	23.1 % (758/3286)	25.0 % (893/3572)	23.2 % (347/1494)	0.13558
>=4 AHDs	11.3 % (941/8352)	10.2 % (336/3286)	11.4 % (408/3572)	13.2 % (197/1494)	0.01027
Fixed-dose combinations					
Fixed-dose combination ARB/calcium channel blocker/diuretic	71.1 % (447/629)	70.1 % (164/234)	72.7 % (205/282)	69.0 % (78/113)	0.70401
Fixed-dose combination ACE inhibitor/diuretic	50.4 % (911/1808)	54.3 % (367/676)	49.8 % (391/785)	44.1 % (153/347)	0.00773
Fixed-dose combination ARB/diuretic	65.2 % (606/930)	66.7 % (238/357)	64.6 % (263/407)	63.3 % (105/166)	0.71343
Fixed-dose combination ARB/calcium channel blocker	37.9 % (186/491)	37.4 % (71/190)	40.4 % (88/218)	32.5 % (27/83)	0.44851
Fixed-dose combination ACE inhibitor/calcium channel blocker	14.2 % (153/1075)	16.0 % (64/400)	12.9 % (58/450)	13.8 % (31/225)	0.42162
Fixed-dose combination direct renin inhibitor/diuretic	56.5 % (13/23)	50.0 % (4/8)	63.6 % (7/11)	50.0 % (2/4)	0.80482
Novartis drugs					
Valsartan / Hydrochlorothiazide					
CoDiovan	32.1 % (69/215)	34.5 % (29/84)	35.7 % (35/98)	15.2 % (5/33)	0.07564
Codiovan forte	14.4 % (31/215)	15.5 % (13/84)	13.3 % (13/98)	15.2 % (5/33)	0.90659
Cordinate plus	1.4 % (3/215)	2.4 % (2/84)	0.0 % (0/98)	3.0 % (1/33)	0.26969
Provas	0.5 % (1/215)	0.0 % (0/84)	1.0 % (1/98)	0.0 % (0/33)	0.54896
Provas comp	6.5 % (14/215)	6.0 % (5/84)	6.1 % (6/98)	9.1 % (3/33)	0.80728
Provas maxx	1.9 % (4/215)	1.2 % (1/84)	3.1 % (3/98)	0.0 % (0/33)	0.44799
Other	43.3 % (93/215)	40.5 % (34/84)	40.8 % (40/98)	57.6 % (19/33)	0.19603
Valsartan					
Cordinate	4.0 % (13/322)	3.7 % (5/136)	4.3 % (6/140)	4.3 % (2/46)	0.96105
Diovan	34.8 % (112/322)	34.6 % (47/136)	32.9 % (46/140)	41.3 % (19/46)	0.57859

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
Provas	7.1 % (23/322)	5.9 % (8/136)	7.9 % (11/140)	8.7 % (4/46)	0.74056
Other	54.0 % (174/322)	55.9 % (76/136)	55.0 % (77/140)	45.7 % (21/46)	0.46282
Valsartan / Amlodipine / Hydrochlorothiazide					
Exforge HCT	77.0 % (164/213)	81.9 % (68/83)	75.8 % (69/91)	69.2 % (27/39)	0.28112
Dafiro HCT	13.1 % (28/213)	8.4 % (7/83)	15.4 % (14/91)	17.9 % (7/39)	0.24641
Other	9.9 % (21/213)	9.6 % (8/83)	8.8 % (8/91)	12.8 % (5/39)	0.77640
Aliskiren					
Rasilez	96.2 % (25/26)	100.0 % (14/14)	100.0 % (7/7)	80.0 % (4/5)	0.11259
Other	3.8 % (1/26)	0.0 % (0/14)	0.0 % (0/7)	20.0 % (1/5)	0.11259
Hydrochlorothiazide					
Esidrix	3.8 % (23/606)	4.7 % (11/234)	3.2 % (8/250)	3.3 % (4/122)	0.65138
Other	96.2 % (583/606)	95.3 % (223/234)	96.8 % (242/250)	96.7 % (118/122)	0.65138
Aliskiren / Hydrochlorothiazide					
Rasilez HCT	92.3 % (12/13)	75.0 % (3/4)	100.0 % (7/7)	100.0 % (2/2)	0.29560
Other	7.7 % (1/13)	25.0 % (1/4)	0.0 % (0/7)	0.0 % (0/2)	0.29560
Valsartan / Amlodipine					
Exforge	79.2 % (84/106)	73.5 % (25/34)	80.8 % (42/52)	85.0 % (17/20)	0.56228
Dafiro	16.0 % (17/106)	20.6 % (7/34)	13.5 % (7/52)	15.0 % (3/20)	0.67196
Other	4.7 % (5/106)	5.9 % (2/34)	5.8 % (3/52)	0.0 % (0/20)	0.54310

Table 9-21. *Hypoglycemic events in the HbA1c treatment groups before baseline.*

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
No. of patients	8567 (100.0 %)	3342 (39.0 %)	3625 (42.3 %)	1600 (18.7 %)	
Without specific symptoms	3.5 % (282/8094)	2.7 % (85/3187)	3.7 % (127/3471)	4.9 % (70/1436)	0.00058
No. of events	3.68 ± 4.65, n=277	3.81 ± 5.67, n=85	3.81 ± 4.51, n=126	3.26 ± 3.33, n=66	0.80036
Symptomatic, but controllable without external help	3.8 % (314/8182)	3.0 % (98/3220)	4.2 % (147/3507)	4.7 % (69/1455)	0.00701
No. of events	3.79 ± 4.60, n=308	3.45 ± 3.40, n=97	3.99 ± 4.81, n=146	3.83 ± 5.62, n=65	0.04824
External help needed	0.7 % (54/8202)	0.4 % (14/3227)	0.6 % (21/3512)	1.3 % (19/1463)	0.00267
No. of events	2.81 ± 2.50, n=54	3.07 ± 2.34, n=14	3.19 ± 2.42, n=21	2.21 ± 2.72, n=19	0.11890
Symptomatic with medical help	0.7 % (55/8211)	1.0 % (32/3226)	0.5 % (17/3521)	0.4 % (6/1464)	0.01523
No. of events	4.04 ± 2.83, n=55	3.69 ± 2.69, n=32	5.12 ± 3.16, n=17	2.83 ± 1.83, n=6	0.07783
Hospitalization required	0.2 % (13/8257)	0.2 % (6/3250)	0.2 % (7/3536)	0.0 % (0/1471)	0.24152
No. of events	1.08 ± 0.28, n=13	1.00 ± 0.00, n=6	1.14 ± 0.38, n=7	, n=0	0.44040[U]

Table 9-22. *Patient-reported outcomes regarding diabetes and hypertension in the HbA1c treatment groups at baseline.*

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
No. of patients	8567 (100.0 %)	3342 (39.0 %)	3625 (42.3 %)	1600 (18.7 %)	
Antidiabetic therapy: impact on weight					
No change in weight	65.1 % (3282/5044)	66.5 % (1323/1989)	64.0 % (1407/2197)	64.3 % (552/858)	0.21713
Weight gain	24.4 % (1233/5044)	23.6 % (470/1989)	25.1 % (552/2197)	24.6 % (211/858)	0.52842
Weight loss	10.5 % (529/5044)	9.9 % (196/1989)	10.8 % (238/2197)	11.1 % (95/858)	0.48637
Symptoms of hypoglycemia under antidiabetic medication					
No symptoms of hypoglycemia	85.3 % (4284/5021)	84.8 % (1680/1980)	86.7 % (1898/2189)	82.9 % (706/852)	0.02010
Once/twice symptoms of hypoglycemia	12.8 % (644/5021)	13.2 % (261/1980)	11.5 % (252/2189)	15.4 % (131/852)	0.01386
Weekly symptoms of hypoglycemia	1.9 % (93/5021)	2.0 % (39/1980)	1.8 % (39/2189)	1.8 % (15/852)	0.88264
Continuity of antidiabetic medication within last 12 months					
Continuous antidiabetic medication	71.8 % (3548/4941)	74.2 % (1444/1945)	71.5 % (1544/2158)	66.8 % (560/838)	0.00033
Non-continuous antidiabetic medication	28.2 % (1393/4941)	25.8 % (501/1945)	28.5 % (614/2158)	33.2 % (278/838)	0.00033
Continuity of antihypertensive medication within last 12 months					
Continuous antihypertensive medication	83.3 % (4090/4911)	82.5 % (1596/1935)	84.1 % (1804/2144)	82.9 % (690/832)	0.34927
Non-continuous antihypertensive medication	16.7 % (821/4911)	17.5 % (339/1935)	15.9 % (340/2144)	17.1 % (142/832)	0.34927
No. of tablets for diabetes and hypertension					
1 - 3 tablets	48.1 % (2417/5021)	51.2 % (1014/1981)	45.2 % (989/2188)	48.6 % (414/852)	0.00055
4 - 6 tablets	42.4 % (2129/5021)	40.3 % (799/1981)	44.9 % (982/2188)	40.8 % (348/852)	0.00736
7 or more tablets	9.5 % (475/5021)	8.5 % (168/1981)	9.9 % (217/2188)	10.6 % (90/852)	0.13773

Table 9-23. *Quality of life (EQ-5D) data in the HbA1c treatment groups at baseline.*

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
No. of patients	8567 (100.0 %)	3342 (39.0 %)	3625 (42.3 %)	1600 (18.7 %)	
Mobility					
No problems	73.5 % (3704/5040)	78.7 % (1557/1979)	71.6 % (1577/2203)	66.4 % (570/858)	<.00001
Some problems	26.2 % (1322/5040)	21.1 % (418/1979)	28.2 % (621/2203)	33.0 % (283/858)	<.00001
Confined to bed	0.3 % (14/5040)	0.2 % (4/1979)	0.2 % (5/2203)	0.6 % (5/858)	0.17420
Self-care					
No problems	90.1 % (4535/5035)	92.9 % (1842/1982)	89.0 % (1956/2197)	86.1 % (737/856)	<.00001
Some problems	9.2 % (465/5035)	6.4 % (127/1982)	10.3 % (227/2197)	13.0 % (111/856)	<.00001
Unable	0.7 % (35/5035)	0.7 % (13/1982)	0.6 % (14/2197)	0.9 % (8/856)	0.64991
Usual activities					
No problems	76.9 % (3876/5038)	83.1 % (1648/1982)	74.2 % (1632/2200)	69.6 % (596/856)	<.00001
Some problems	21.9 % (1105/5038)	15.8 % (313/1982)	24.9 % (548/2200)	28.5 % (244/856)	<.00001
Unable	1.1 % (57/5038)	1.1 % (21/1982)	0.9 % (20/2200)	1.9 % (16/856)	0.07322
Pain/discomfort					
None	50.5 % (2538/5026)	56.7 % (1121/1976)	47.9 % (1054/2200)	42.7 % (363/850)	<.00001
Moderate	45.6 % (2290/5026)	39.7 % (785/1976)	47.9 % (1053/2200)	53.2 % (452/850)	<.00001
Extreme	3.9 % (198/5026)	3.5 % (70/1976)	4.2 % (93/2200)	4.1 % (35/850)	0.50267
Anxiety/depression					
Not anxious or depressed	72.9 % (3668/5034)	74.4 % (1475/1983)	72.2 % (1590/2201)	70.9 % (603/850)	0.11447
Moderately anxious or depressed	24.6 % (1238/5034)	22.5 % (447/1983)	25.6 % (564/2201)	26.7 % (227/850)	0.02015
Extremely anxious or depressed	2.5 % (128/5034)	3.1 % (61/1983)	2.1 % (47/2201)	2.4 % (20/850)	0.14412
Health state today	72.0 (60.0, 82.0)	75.0 (60.0, 86.0)	70.0 (60.0, 80.0)	70.0 (57.0, 80.0)	<.00001
EQoL-D5 score acc. to Greiner, 2004	0.88 ± 0.18, n=4968	0.89 ± 0.18, n=1954	0.87 ± 0.18, n=2176	0.86 ± 0.19, n=838	<.00001

9.3.2 SBP treatment target groups

Table 9-24 shows multivariate predictors for a loose treatment target in the SBP treatment target groups (i.e. SBP target of >135 – - ≤ 140 mmHg): factors assessed at baseline contributing to the assignment of patients into the loose target group for SBP.

Table 9-25 shows patient characteristics in the SBP treatment groups at baseline (i.e. Gender; Age; Blood pressure at admission; Heart rate; Weight; Height; Body-Mass-Index; Waist circumference; Level of care needed; Social status; Education; Smoking status and alcohol consumption; Physical exercise).

Table 9-26 shows comorbid diseases in the SBP treatment groups at baseline (i.e. Vascular concomitant diseases; Other diabetes-related diseases; History of amputation; Other concomitant diseases).

Table 9-27 shows available laboratory values at baseline (not older than 6 weeks) in the SBP treatment groups (i.e. Cholesterol; Glucose; Haemoglobin; Creatinine; Liver function)

Table 9-28 shows therapeutic patterns in the SBP treatment groups at baseline: previous antidiabetic therapy (i.e. Metformin; Sulfonylurea drugs; Glucosidase inhibitors; Glinide; Glitazone; DPP-4 inhibitors; SGTL-2 inhibitors; Novartis drugs).

Table 9-29 shows the reasons for pharmacotherapy change in the SBP treatment groups at baseline.

Table 9-30 shows therapeutic patterns in the SBP treatment groups at baseline: current anti-diabetic therapy (i.e. Metformin; Sulfonylurea drugs; Glucosidase inhibitors; Glinide; Glitazone; DPP-4 inhibitors; GLP-1 analogs; SGTL-2 inhibitors; Total number of antidiabetics; Insulin; Novartis drugs).

Table 9-31 shows therapeutic patterns in the SBP treatment groups at baseline: current anti-hypertensive therapy (i.e. ACE inhibitors; ARB; Direct renin inhibitor; Beta-blocker; Calcium channel blocker; Diuretic drugs; Total number of antihypertensive drugs; Fixed-dose combinations; Novartis drugs).

Table 9-32 shows hypoglycemic events in the SBP treatment groups before baseline (i.e. Number of events; Type of events; Help needed).

Table 9-33 shows patient reported outcomes regarding diabetes and hypertension in the SBP treatment groups at baseline (i.e. Impact on weight; Symptoms; Continuity of medication; Number of tablets).

Table 9-34 shows Quality of Life data (EQ-5D) in the SBP treatment groups at baseline (i.e. Mobility; Self-care; Usual activities; Pain/discomfort; Anxiety/depression; Health status; EQoL-5D score).

Table 9-24. *Multivariate adjusted predictors for choosing a loose treatment target (SBP >135 to ≤ 140 mmHg)*

	Odds Ratio Estimate	95% Confidence Interval	
Age (years) (≥ vs. < median)	**1.413**	**1.250**	**1.598**
Female sex (%)	0.979	0.874	1.097
BMI (kg/m^2) (≥ vs. < median)	1.046	0.932	1.173
Fasting blood glucose (mmol/l) (≥ vs. < median)	**1.341**	**1.187**	**1.516**
Current smoker (%)	1.028	0.859	1.230
Diabetes duration (years) (≥ vs. < median)	1.045	0.931	1.173
HbA1c (%)(≥ vs. < median)	1.067	0.938	1.214
Systolic BP (mmHg) (≥ vs. < median)	**2.649**	**2.352**	**2.983**
Prior myocardial infarction (yes vs. no)	0.868	0.703	1.072
Prior stroke/TIA (yes vs. no)	0.917	0.726	1.157
Heart failure (yes vs. no)	**1.529**	**1.302**	**1.795**
Peripheral arterial disease (yes vs. no)	**1.500**	**1.204**	**1.868**
Neuropathy (yes vs. no)	**0.816**	**0.686**	**0.971**
Non-proliferative diabetic retinopathy (yes vs. no)	0.764	0.575	1.016

Table 9-25. *Patient characteristics in the SBP treatment groups at baseline*.

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
No. of patients	8536 (100.0 %)	3319 (38.9 %)	2853 (33.4 %)	2364 (27.7 %)	
Sociodemographics					
Women	45.5 % (3881/8536)	46.1 % (1530/3319)	44.7 % (1274/2853)	45.6 % (1077/2364)	0.52192
Age at baseline [years]	65.07 ± 11.34, n=8536	63.32 ± 11.69, n=3319	65.77 ± 10.84, n=2853	66.67 ± 11.12, n=2364	<.00001
MEDIAN	65 (57, 74)	64 (55, 72)	66 (58, 74)	68 (59, 75)	
RANGE	19 , 97	19 , 93	20 , 97	26 , 93	
Age > 75yrs	19.7 % (1680/8536)	16.7 % (554/3319)	20.5 % (586/2853)	22.8 % (540/2364)	<.00001
Systolic blood pressure at admission	140.22 ± 15.65, n=8367	136.36 ± 15.46, n=3281	140.71 ± 14.77, n=2813	145.18 ± 15.49, n=2273	<.00001
Median	140.0 (130.0, 150.0)	135.0 (128.0, 145.0)	140.0 (130.0, 150.0)	142.0 (138.0, 151.0)	
RANGE	90.0 , 250.0	90.0 , 211.0	96.0 , 250.0	94.0 , 223.0	
[SBP - target]	5.81 ± 15.24, n=8364	6.36 ± 15.46, n=3280	5.71 ± 14.77, n=2813	5.16 ± 15.47, n=2271	0.02056
Diastolic blood pressure at admission	82.60 ± 9.46, n=8366	81.28 ± 9.46, n=3280	82.97 ± 9.08, n=2813	84.06 ± 9.68, n=2273	<.00001
Median	80.0 (80.0, 90.0)	80.0 (76.0, 87.0)	80.0 (80.0, 90.0)	84.0 (80.0, 90.0)	
RANGE	30.0 , 140.0	35.0 , 118.0	42.0 , 140.0	30.0 , 120.0	
[DBP - target]	-0.95 ± 9.51, n=8366	0.87 ± 9.42, n=3280	-1.25 ± 9.06, n=2813	-3.23 ± 9.64, n=2273	<.00001
Heart rate [/min]	75.03 ± 10.02, n=8318	74.48 ± 10.18, n=3256	75.20 ± 9.60, n=2802	75.61 ± 10.24, n=2260	<.00001
Median	74.0 (68.0, 80.0)	72.0 (68.0, 80.0)	75.0 (68.0, 80.0)	75.0 (69.0, 80.0)	
RANGE	33.0 , 144.0	33.0 , 130.0	44.0 , 126.0	43.0 , 144.0	
Weight [kg]	90.32 ± 18.44, n=8372	90.21 ± 18.56, n=3281	90.50 ± 18.05, n=2819	90.26 ± 18.74, n=2272	0.57357
Median	88.0 (78.0, 100.0)	88.0 (78.0, 100.0)	88.0 (79.0, 100.0)	88.0 (78.0, 100.0)	
RANGE	43.0 , 203.0	45.0 , 199.0	45.0 , 203.0	43.0 , 187.0	
Height [cm]	170.02 ± 9.18, n=8368	170.19 ± 9.31, n=3281	170.23 ± 9.07, n=2815	169.53 ± 9.11, n=2272	0.01200
Median	170.0 (164.0, 176.0)	170.0 (164.0, 177.0)	170.0 (164.0, 176.0)	170.0 (163.0, 176.0)	
RANGE	104.0 , 200.0	104.0 , 198.0	128.0 , 200.0	136.0 , 198.0	
BMI [kg/m2]	31.21 ± 5.82, n=8366	31.11 ± 5.83, n=3280	31.19 ± 5.65, n=2814	31.38 ± 6.00, n=2272	0.43540
Median	30.1 (27.2, 34.3)	30.1 (27.2, 34.2)	30.2 (27.3, 34.2)	30.4 (27.1, 34.5)	

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
RANGE	15.8 , 85.1	17.4 , 85.1	18.3 , 70.2	15.8 , 69.3	
BMI < 25	10.2 % (855/8366)	11.1 % (364/3280)	9.4 % (264/2814)	10.0 % (227/2272)	0.08054
BMI: 25 - 30	37.7 % (3155/8366)	37.5 % (1230/3280)	38.6 % (1085/2814)	37.0 % (840/2272)	0.48470
BMI > 30	52.1 % (4356/8366)	51.4 % (1686/3280)	52.1 % (1465/2814)	53.0 % (1205/2272)	0.48749
Waist circumference [cm]	107.64 ± 14.40, n=3222	107.92 ± 14.92, n=1237	107.40 ± 13.70, n=1229	107.59 ± 14.64, n=756	0.60264
Median	106.0 (98.0, 116.0)	107.0 (98.0, 117.0)	106.0 (98.0, 115.0)	106.0 (98.0, 117.0)	
RANGE	62.0 , 190.0	62.0 , 174.0	66.0 , 190.0	64.0 , 169.0	
Known diabetes [years]	6.90 ± 5.63, n=8282	6.49 ± 5.58, n=3245	7.17 ± 5.80, n=2790	7.17 ± 5.47, n=2247	<.00001
Participation in diabetes training	72.1 % (6034/8368)	72.8 % (2388/3282)	74.5 % (2096/2815)	68.3 % (1550/2271)	<.00001
Participation in DMP for diabetes	85.2 % (7133/8370)	86.9 % (2853/3282)	84.0 % (2366/2815)	84.2 % (1914/2273)	0.00191
Health insurance	98.1 % (8371/8536)	98.9 % (3282/3319)	98.7 % (2816/2853)	96.2 % (2273/2364)	<.00001
Statutory health insurance	96.2 % (8056/8371)	96.5 % (3168/3282)	95.0 % (2676/2816)	97.3 % (2212/2273)	0.00006
Private health insurance	3.8 % (315/8371)	3.5 % (114/3282)	5.0 % (140/2816)	2.7 % (61/2273)	0.00006
In need of care	2.6 % (219/8364)	1.6 % (54/3281)	2.6 % (74/2812)	4.0 % (91/2271)	<.00001
Level 1 of care	84.9 % (186/219)	85.2 % (46/54)	86.5 % (64/74)	83.5 % (76/91)	0.86723
Level 2 of care	13.7 % (30/219)	14.8 % (8/54)	12.2 % (9/74)	14.3 % (13/91)	0.89083
Level 3 of care	1.4 % (3/219)	0.0 % (0/54)	1.4 % (1/74)	2.2 % (2/91)	0.54556
Social status					
Employed	30.7 % (2572/8367)	36.0 % (1182/3281)	28.6 % (804/2813)	25.8 % (586/2273)	<.00001
Economically inactive	64.1 % (5364/8367)	59.0 % (1936/3281)	66.5 % (1870/2813)	68.5 % (1558/2273)	<.00001
Unemployed	13.1 % (702/5364)	14.1 % (273/1936)	14.1 % (264/1870)	10.6 % (165/1558)	0.00244
Housewife/househusband	4.8 % (260/5364)	5.2 % (100/1936)	5.0 % (93/1870)	4.3 % (67/1558)	0.47256
Retirement	81.1 % (4349/5364)	79.5 % (1539/1936)	80.1 % (1498/1870)	84.2 % (1312/1558)	0.00079
Incapable of working	1.0 % (53/5364)	1.2 % (24/1936)	0.8 % (15/1870)	0.9 % (14/1558)	0.36041
Other status	0.7 % (62/8367)	0.8 % (25/3281)	0.7 % (19/2813)	0.8 % (18/2273)	0.87630
Status unknown	4.4 % (369/8367)	4.2 % (138/3281)	4.3 % (120/2813)	4.9 % (111/2273)	0.43372
Patient lives alone	20.4 % (1707/8350)	18.0 % (589/3267)	21.6 % (608/2811)	22.4 % (510/2272)	0.00005

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
Education					
1-8 years at school	31.5 % (2635/8364)	29.3 % (962/3280)	34.1 % (959/2812)	31.4 % (714/2272)	0.00033
9-12 years at school	23.6 % (1975/8364)	22.9 % (750/3280)	25.5 % (717/2812)	22.4 % (508/2272)	0.01402
Commercial / technical school	7.8 % (651/8364)	8.2 % (268/3280)	8.5 % (238/2812)	6.4 % (145/2272)	0.01281
University	4.3 % (358/8364)	4.3 % (140/3280)	4.4 % (123/2812)	4.2 % (95/2272)	0.94371
Unknown	32.8 % (2745/8364)	35.4 % (1160/3280)	27.6 % (775/2812)	35.7 % (810/2272)	<.00001
Smoker	11.7 % (976/8345)	12.1 % (394/3264)	11.5 % (322/2809)	11.4 % (260/2272)	0.69345
Ex-smoker	15.2 % (1271/8345)	14.6 % (478/3264)	16.8 % (472/2809)	14.1 % (321/2272)	0.01510
Non-smoker	73.1 % (6098/8345)	73.3 % (2392/3264)	71.7 % (2015/2809)	74.4 % (1691/2272)	0.09282
Alcohol consumption	61.9 % (5161/8340)	60.4 % (1968/3260)	64.4 % (1808/2808)	61.0 % (1385/2272)	0.00325
Monthly	47.0 % (2426/5161)	47.0 % (924/1968)	44.9 % (812/1808)	49.8 % (690/1385)	0.02251
Weekly	40.3 % (2082/5161)	39.9 % (786/1968)	43.1 % (780/1808)	37.3 % (516/1385)	0.00318
Daily	12.7 % (653/5161)	13.1 % (258/1968)	11.9 % (216/1808)	12.9 % (179/1385)	0.52748
Physical exercise					
less than 1 hour/week	33.4 % (2790/8347)	32.9 % (1072/3263)	30.1 % (845/2811)	38.4 % (873/2273)	<.00001
1 hour/week	18.1 % (1513/8347)	16.7 % (544/3263)	17.9 % (504/2811)	20.5 % (465/2273)	0.00147
2 hours/week	17.9 % (1496/8347)	17.5 % (571/3263)	20.3 % (570/2811)	15.6 % (355/2273)	0.00007
3 hours/week	13.2 % (1103/8347)	14.4 % (469/3263)	14.8 % (415/2811)	9.6 % (219/2273)	<.00001
4 hours/week	7.0 % (585/8347)	7.4 % (242/3263)	7.0 % (196/2811)	6.5 % (147/2273)	0.39441
5 hours/week	4.0 % (332/8347)	4.3 % (141/3263)	3.8 % (107/2811)	3.7 % (84/2273)	0.42796
6 hours/week	2.1 % (178/8347)	2.2 % (72/3263)	2.0 % (55/2811)	2.2 % (51/2273)	0.72715
7 hours/week	1.6 % (133/8347)	1.6 % (53/3263)	1.6 % (46/2811)	1.5 % (34/2273)	0.90889
8 hours/week	0.7 % (59/8347)	1.0 % (32/3263)	0.5 % (15/2811)	0.5 % (12/2273)	0.05713
9 or more hours/week	1.9 % (158/8347)	2.1 % (67/3263)	2.1 % (58/2811)	1.5 % (33/2273)	0.19466

Table 9-26. *Comorbid diseases in the SBP treatment groups at baseline*

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
Vascular concomitant diseases	34.2 % (2921/8536)	31.6 % (1050/3319)	35.3 % (1008/2853)	36.5 % (863/2364)	0.00021
Coronary Heart Disease	23.9 % (1992/8325)	23.5 % (764/3254)	24.0 % (674/2807)	24.5 % (554/2264)	0.69185
History of myocardial infarction	8.3 % (693/8323)	8.2 % (266/3254)	9.1 % (256/2806)	7.6 % (171/2263)	0.12301
History of PCI	6.7 % (556/8320)	6.8 % (221/3252)	6.9 % (194/2805)	6.2 % (141/2263)	0.59052
History of CABG	3.6 % (299/8321)	3.4 % (111/3253)	4.2 % (118/2805)	3.1 % (70/2263)	0.08255
History of stroke/TIA	6.1 % (508/8321)	5.2 % (169/3252)	6.8 % (192/2806)	6.5 % (147/2263)	0.01883
Heart Failure	13.4 % (1117/8322)	11.5 % (375/3252)	12.9 % (361/2806)	16.8 % (381/2264)	<.00001
NYHA I	34.8 % (388/1116)	34.9 % (131/375)	35.8 % (129/360)	33.6 % (128/381)	0.81241
NYHA II	58.0 % (647/1116)	58.4 % (219/375)	55.8 % (201/360)	59.6 % (227/381)	0.57453
NYHA III	6.5 % (73/1116)	6.1 % (23/375)	7.5 % (27/360)	6.0 % (23/381)	0.66965
NYHA IV	0.7 % (8/1116)	0.5 % (2/375)	0.8 % (3/360)	0.8 % (3/381)	0.87252
Peripheral arterial occlusive disease	6.8 % (564/8321)	4.9 % (158/3253)	7.5 % (210/2805)	8.7 % (196/2263)	<.00001
Other and/or diabetes-related diseases	84.8 % (7242/8536)	82.9 % (2752/3319)	87.1 % (2485/2853)	84.8 % (2005/2364)	0.00003
Dyslipidemia	57.8 % (4814/8324)	55.1 % (1793/3253)	58.3 % (1635/2806)	61.2 % (1386/2265)	0.00003
Autonomous neuropathy	12.7 % (1058/8331)	11.5 % (374/3254)	14.3 % (400/2807)	12.5 % (284/2270)	0.00544
Non-proliferative diabetic retinopathy	4.2 % (352/8340)	4.1 % (133/3267)	4.7 % (131/2807)	3.9 % (88/2266)	0.33271
Proliferative diabetic retinopathy / laser coagulation	1.1 % (89/8338)	0.9 % (28/3267)	1.1 % (31/2806)	1.3 % (30/2265)	0.24369
Diabetic macular edema	0.8 % (65/7942)	0.4 % (12/3127)	1.3 % (34/2661)	0.9 % (19/2154)	0.00078
Ophthalmologist consultation	71.1 % (5929/8339)	67.4 % (2202/3267)	74.3 % (2085/2807)	72.5 % (1642/2265)	<.00001
Blindness	0.4 % (30/8352)	0.5 % (15/3273)	0.4 % (10/2809)	0.2 % (5/2270)	0.34592
Dialysis	0.1 % (8/8354)	0.2 % (5/3274)	0.0 % (1/2808)	0.1 % (2/2272)	0.33517
History of amputation	0.6 % (47/8536)	0.5 % (15/3319)	0.4 % (11/2853)	0.9 % (21/2364)	0.03122
Foot	14.9 % (7/47)	20.0 % (3/15)	27.3 % (3/11)	4.8 % (1/21)	0.18833
Toes	57.4 % (27/47)	53.3 % (8/15)	72.7 % (8/11)	52.4 % (11/21)	0.50284
Lower extremities	25.5 % (12/47)	33.3 % (5/15)	0.0 % (0/11)	33.3 % (7/21)	0.08527
Upper extremities	6.4 % (3/47)	0.0 % (0/15)	9.1 % (1/11)	9.5 % (2/21)	0.47133

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
Other concomitant diseases	46.0 % (3834/8337)	42.6 % (1387/3259)	46.0 % (1293/2808)	50.8 % (1154/2270)	<.00001

Table 9-27. *Available laboratory values at baseline (not older than 6 weeks) in the SBP treatment groups*

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
No. of patients	8536 (100.0 %)	3319 (38.9 %)	2853 (33.4 %)	2364 (27.7 %)	
Laboratory values (last 6 weeks)					
Total fasting cholesterol available	82.9 % (7073/8536)	83.2 % (2762/3319)	84.3 % (2406/2853)	80.6 % (1905/2364)	0.00131
Total fasting cholesterol [mmol/L]	5.31 ± 1.21, n=7073	5.27 ± 1.16, n=2762	5.29 ± 1.19, n=2406	5.39 ± 1.31, n=1905	0.02735
Fasting HDL-cholesterol available	70.5 % (6015/8536)	70.6 % (2344/3319)	72.2 % (2060/2853)	68.1 % (1611/2364)	0.00582
Fasting HDL-cholesterol [mmol/L]	1.26 ± 0.40, n=6015	1.27 ± 0.40, n=2344	1.26 ± 0.40, n=2060	1.26 ± 0.40, n=1611	0.42642
Fasting LDL-cholesterol available	69.9 % (5970/8536)	70.5 % (2339/3319)	71.4 % (2036/2853)	67.5 % (1595/2364)	0.00655
Fasting LDL-cholesterol [mmol/L]	3.20 ± 1.01, n=5970	3.14 ± 1.01, n=2339	3.21 ± 0.98, n=2036	3.28 ± 1.05, n=1595	0.00007
Fasting triglycerides available	74.1 % (6323/8536)	74.8 % (2482/3319)	76.0 % (2168/2853)	70.8 % (1673/2364)	0.00005
Fasting triglycerides [mmol/L]	2.32 ± 1.64, n=6323	2.28 ± 1.70, n=2482	2.31 ± 1.57, n=2168	2.39 ± 1.62, n=1673	0.00525
Fasting glucose available	83.1 % (7093/8536)	83.8 % (2781/3319)	85.5 % (2439/2853)	79.2 % (1873/2364)	<.00001
Fasting glucose [mmol/L]	8.51 ± 2.78, n=7093	8.15 ± 2.72, n=2781	8.69 ± 2.75, n=2439	8.83 ± 2.86, n=1873	<.00001
Postprandial glucose available	48.8 % (4166/8536)	49.2 % (1634/3319)	52.6 % (1500/2853)	43.7 % (1032/2364)	<.00001
Postprandial glucose [mmol/L]	10.87 ± 3.40, n=4166	10.47 ± 3.20, n=1634	11.13 ± 3.40, n=1500	11.12 ± 3.64, n=1032	<.00001
Hb1Ac available	94.6 % (8072/8536)	95.2 % (3161/3319)	95.8 % (2733/2853)	92.1 % (2178/2364)	<.00001
HbA1c [%]	7.80 ± 2.13, n=8072	7.52 ± 1.37, n=3161	7.91 ± 1.37, n=2733	8.07 ± 3.40, n=2178	<.00001
Haemoglobin available	60.3 % (5146/8536)	61.2 % (2031/3319)	62.8 % (1791/2853)	56.0 % (1324/2364)	<.00001
Haemoglobin [mmol/L]	8.26 ± 1.45, n=5146	8.19 ± 1.47, n=2031	8.27 ± 1.52, n=1791	8.36 ± 1.33, n=1324	0.00784
Serum creatinine available	82.5 % (7042/8536)	83.4 % (2768/3319)	84.4 % (2408/2853)	78.9 % (1866/2364)	<.00001
Serum creatinine [µmol/l]	85.54 ± 57.01, n=7042	86.55 ± 75.21, n=2768	84.07 ± 38.80, n=2408	85.94 ± 43.96, n=1866	0.02744
eGFR according to MDRD formula [ml/min]	81.82 ± 24.54, n=7042	83.00 ± 25.45, n=2768	81.52 ± 23.46, n=2408	80.44 ± 24.46, n=1866	0.00221
Microalbustix albumin [mg/l]	32.18 ± 37.45, n=1546	30.79 ± 37.07, n=598	32.29 ± 35.44, n=591	34.34 ± 41.16, n=357	0.23014
Microalbustix creatinine [mg/dl]	56.80 ± 77.46, n=798	51.25 ± 71.58, n=316	53.01 ± 71.36, n=301	72.78 ± 93.67, n=181	0.06299

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
Macroalbuminuria: positive test	10.5 % (587/5602)	10.5 % (230/2181)	9.8 % (189/1922)	11.2 % (168/1499)	0.42485
Macroalbuminuria: negative test	89.5 % (5015/5602)	89.5 % (1951/2181)	90.2 % (1733/1922)	88.8 % (1331/1499)	0.42485
Increased liver function readings	19.6 % (1234/6287)	18.6 % (463/2492)	19.2 % (416/2165)	21.8 % (355/1630)	0.03418

Table 9-28. *Previous antidiabetic therapy in the SBP treatment groups at baseline.*

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
No. of patients	8536 (100.0 %)	3319 (38.9 %)	2853 (33.4 %)	2364 (27.7 %)	
Metformin	79.9 % (6662/8342)	79.8 % (2605/3265)	81.7 % (2296/2811)	77.7 % (1761/2266)	0.00215
Metformin, dosage [mg/day]	1618.41 ± 582.16, n=6642	1605.41 ± 583.31, n=2588	1649.69 ± 565.00, n=2294	1596.77 ± 600.82, n=1760	0.00702
Duration of metformin treatment [yrs]	3.2 (1.4, 6.1)	3.0 (1.3, 5.7)	3.5 (1.6, 6.5)	3.2 (1.3, 6.2)	<.00001
Sulfonylurea drugs	23.9 % (1993/8331)	21.0 % (683/3260)	25.9 % (727/2807)	25.8 % (583/2264)	<.00001
Sulfonylurea drugs, dosage [mg/day]	3.40 ± 1.90, n=1992	3.28 ± 1.85, n=682	3.55 ± 1.98, n=727	3.36 ± 1.87, n=583	0.05938
Duration of sulfonylurea treatment [yrs]	3.5 (1.6, 6.4)	3.3 (1.6, 5.8)	3.5 (1.7, 6.3)	3.6 (1.5, 6.9)	0.18765
Substance					
Carbutamide	0.0 % (0/1993)	0.0 % (0/683)	0.0 % (0/727)	0.0 % (0/583)	
Tolbutamide	0.0 % (0/1993)	0.0 % (0/683)	0.0 % (0/727)	0.0 % (0/583)	
Glibenclamide	25.5 % (509/1993)	23.9 % (163/683)	25.4 % (185/727)	27.6 % (161/583)	0.31168
Glibornuride	0.0 % (0/1993)	0.0 % (0/683)	0.0 % (0/727)	0.0 % (0/583)	
Gliclazide	0.1 % (1/1993)	0.1 % (1/683)	0.0 % (0/727)	0.0 % (0/583)	0.38309
Glipizide	0.0 % (0/1993)	0.0 % (0/683)	0.0 % (0/727)	0.0 % (0/583)	
Gliquidone	0.4 % (7/1993)	0.1 % (1/683)	0.7 % (5/727)	0.2 % (1/583)	0.15653
Glisoxepide	0.0 % (0/1993)	0.0 % (0/683)	0.0 % (0/727)	0.0 % (0/583)	
Glycodiazine	0.3 % (5/1993)	0.7 % (5/683)	0.0 % (0/727)	0.0 % (0/583)	0.00817
Glimepiride	73.1 % (1457/1993)	74.5 % (509/683)	73.2 % (532/727)	71.4 % (416/583)	0.44717
Other	0.7 % (14/1993)	0.6 % (4/683)	0.7 % (5/727)	0.9 % (5/583)	0.84489
Glucosidase inhibitors	2.4 % (196/8330)	2.3 % (74/3259)	2.7 % (76/2807)	2.0 % (46/2264)	0.26603
Glucosidase inhibitors, dosage [mg/day]	146.81 ± 86.49, n=196	145.54 ± 85.65, n=74	156.58 ± 89.20, n=76	132.70 ± 83.00, n=46	0.32504
Duration of treatment with glucosidase inhibitors [yrs]	2.6 (1.1, 6.1)	2.8 (1.0, 5.9)	2.4 (1.3, 6.2)	3.0 (1.2, 5.8)	0.78744
Substance					
Acarbose	92.3 % (181/196)	94.6 % (70/74)	94.7 % (72/76)	84.8 % (39/46)	0.08771
Miglitol	5.6 % (11/196)	1.4 % (1/74)	5.3 % (4/76)	13.0 % (6/46)	0.02536
Other	2.0 % (4/196)	4.1 % (3/74)	0.0 % (0/76)	2.2 % (1/46)	0.21356
Glinide	3.2 % (263/8325)	3.0 % (98/3254)	3.5 % (97/2807)	3.0 % (68/2264)	0.54414

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
Glinide, dosage [mg/day]	23.90 ± 73.50, n=263	34.03 ± 92.24, n=98	10.31 ± 27.88, n=97	28.68 ± 85.15, n=68	0.28685
Duration of glinide treatment [yrs]	2.6 (1.1, 5.6)	3.0 (1.5, 5.5)	2.6 (1.2, 5.3)	2.2 (0.7, 6.4)	0.65677
Substance					
Nateglinide	8.0 % (21/263)	10.2 % (10/98)	5.2 % (5/97)	8.8 % (6/68)	0.41075
Repaglinide	86.7 % (228/263)	84.7 % (83/98)	90.7 % (88/97)	83.8 % (57/68)	0.33464
Other	5.3 % (14/263)	5.1 % (5/98)	4.1 % (4/97)	7.4 % (5/68)	0.65629
Glitazone	1.4 % (120/8331)	1.3 % (42/3259)	1.9 % (54/2808)	1.1 % (24/2264)	0.02420
Glitazone, dosage [mg/day]	30.65 ± 12.37, n=119	32.81 ± 10.60, n=42	32.00 ± 12.68, n=53	23.88 ± 12.68, n=24	0.02761
Duration of glitazone treatment [yrs]	3.8 (2.4, 5.4)	3.5 (1.8, 5.2)	3.7 (2.7, 5.1)	5.0 (3.0, 7.2)	0.06522
Substance					
Pioglitazon	88.2 % (105/119)	97.6 % (41/42)	86.8 % (46/53)	75.0 % (18/24)	0.02108
Other	11.8 % (14/119)	2.4 % (1/42)	13.2 % (7/53)	25.0 % (6/24)	0.02108
DPP-4 inhibitors	17.8 % (1478/8322)	17.5 % (568/3250)	17.8 % (501/2807)	18.1 % (409/2265)	0.84772
DPP-4 inhibitors, dosage [mg/day]	84.61 ± 35.22, n=1477	84.61 ± 36.80, n=568	85.39 ± 31.46, n=501	83.66 ± 37.33, n=408	0.31976
Duration of DPP-4 inhibitor treatment [yrs]	1.4 (0.6, 2.4)	1.5 (0.6, 2.4)	1.4 (0.6, 2.3)	1.4 (0.5, 2.4)	0.52686
Substance					
Sitagliptin	49.0 % (723/1477)	49.3 % (280/568)	48.7 % (244/501)	48.8 % (199/408)	0.97801
Vildagliptin	44.7 % (660/1477)	44.9 % (255/568)	44.3 % (222/501)	44.9 % (183/408)	0.97872
Linagliptin	0.0 % (0/1477)	0.0 % (0/568)	0.0 % (0/501)	0.0 % (0/408)	
Saxagliptin	5.8 % (86/1477)	5.1 % (29/568)	6.4 % (32/501)	6.1 % (25/408)	0.63991
Other	0.5 % (8/1477)	0.7 % (4/568)	0.6 % (3/501)	0.2 % (1/408)	0.61412
SGTL-2 inhibitors	0.2 % (16/8323)	0.2 % (8/3252)	0.1 % (3/2807)	0.2 % (5/2264)	0.43768
SGTL-2 inhibitors, dosage [mg/day]	17.56 ± 24.26, n=16	9.50 ± 1.41, n=8	8.33 ± 2.89, n=3	36.00 ± 39.75, n=5	0.09006
Duration of SGTL-2 inhibitor treatment [yrs]	0.3 (0.2, 0.8)	0.3 (0.2, 1.6)	0.2 (0.1, 2.5)	0.3 (0.2, 0.4)	0.51225
Substance					
Dapagliflozin	68.8 % (11/16)	75.0 % (6/8)	66.7 % (2/3)	60.0 % (3/5)	0.84802
Other	31.3 % (5/16)	25.0 % (2/8)	33.3 % (1/3)	40.0 % (2/5)	0.84802
Fixed-dose combination metformin / DPP-4 inhibitor	77.5 % (911/1175)	77.5 % (347/448)	76.9 % (313/407)	78.4 % (251/320)	0.88505

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
Novartis drugs					
Vildagliptin / Metformin					
Eucreas	85.7 % (396/462)	85.2 % (150/176)	84.1 % (132/157)	88.4 % (114/129)	0.57057
Icandra	14.3 % (66/462)	14.8 % (26/176)	15.9 % (25/157)	11.6 % (15/129)	0.57057
Vildagliptin					
Galvus	68.2 % (135/198)	68.4 % (54/79)	67.7 % (44/65)	68.5 % (37/54)	0.99447
Jalra	31.8 % (63/198)	31.6 % (25/79)	32.3 % (21/65)	31.5 % (17/54)	0.99447
Nateglinide					
STARLIX	95.2 % (20/21)	100.0 % (10/10)	80.0 % (4/5)	100.0 % (6/6)	0.18637
Other	4.8 % (1/21)	0.0 % (0/10)	20.0 % (1/5)	0.0 % (0/6)	0.18637

Table 9-29. *Reasons for pharmacotherapy change in the SBP treatment groups at baseline.*

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
No. of patients	8536 (100.0 %)	3319 (38.9 %)	2853 (33.4 %)	2364 (27.7 %)	
Blood glucose adjustment	87.9 % (7307/8314)	87.9 % (2850/3242)	89.5 % (2514/2808)	85.8 % (1943/2264)	0.00030
Weight gain	19.8 % (1644/8314)	20.9 % (679/3242)	21.4 % (600/2808)	16.1 % (365/2264)	<.00001
Hypoglycemia	3.8 % (319/8314)	2.8 % (92/3242)	4.3 % (120/2808)	4.7 % (107/2264)	0.00053
Other reasons	18.9 % (1571/8314)	18.4 % (596/3242)	18.6 % (521/2808)	20.1 % (454/2264)	0.25323

Table 9-30. *Current anti-diabetic therapy in the SBP treatment groups at baseline.*

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
No. of patients	8536 (100.0 %)	3319 (38.9 %)	2853 (33.4 %)	2364 (27.7 %)	
Metformin	80.0 % (6661/8324)	81.8 % (2660/3251)	80.3 % (2257/2809)	77.0 % (1744/2264)	0.00006
Metformin, dosage [mg/day]	1712.38 ± 540.59, n=6643	1684.91 ± 548.77, n=2647	1751.25 ± 518.14, n=2256	1703.77 ± 553.74, n=1740	0.00003
Sulfonylurea drugs	17.5 % (1460/8320)	15.9 % (517/3251)	18.2 % (511/2807)	19.1 % (432/2262)	0.00481
Sulfonylurea drugs, dosage [mg/day]	3.21 ± 1.90, n=1459	3.21 ± 1.94, n=516	3.24 ± 1.79, n=511	3.16 ± 1.97, n=432	0.34542
Substance					
Carbutamide	0.0 % (0/1459)	0.0 % (0/516)	0.0 % (0/511)	0.0 % (0/432)	
Tolbutamide	0.0 % (0/1459)	0.0 % (0/516)	0.0 % (0/511)	0.0 % (0/432)	
Glibenclamide	21.5 % (313/1459)	25.0 % (129/516)	20.0 % (102/511)	19.0 % (82/432)	0.04751
Glibornuride	0.0 % (0/1459)	0.0 % (0/516)	0.0 % (0/511)	0.0 % (0/432)	
Gliclazide	0.1 % (1/1459)	0.2 % (1/516)	0.0 % (0/511)	0.0 % (0/432)	0.40076
Glipizide	0.0 % (0/1459)	0.0 % (0/516)	0.0 % (0/511)	0.0 % (0/432)	
Gliquidone	0.3 % (5/1459)	0.2 % (1/516)	0.6 % (3/511)	0.2 % (1/432)	0.50031
Glisoxepide	0.1 % (2/1459)	0.4 % (2/516)	0.0 % (0/511)	0.0 % (0/432)	0.16041
Glycodiazine	1.2 % (18/1459)	1.9 % (10/516)	1.0 % (5/511)	0.7 % (3/432)	0.18226
Glimepiride	76.3 % (1113/1459)	71.7 % (370/516)	78.1 % (399/511)	79.6 % (344/432)	0.00837
Other	0.5 % (7/1459)	0.6 % (3/516)	0.4 % (2/511)	0.5 % (2/432)	0.90585
Glucosidase inhibitors	1.1 % (91/8323)	1.1 % (37/3253)	1.3 % (37/2808)	0.8 % (17/2262)	0.14892
Glucosidase inhibitors, dosage [mg/day]	151.62 ± 88.79, n=90	130.97 ± 56.74, n=36	175.17 ± 113.98, n=37	144.12 ± 72.63, n=17	0.32955
Substance					
Acarbose	91.1 % (82/90)	86.1 % (31/36)	94.6 % (35/37)	94.1 % (16/17)	0.39546
Miglitol	7.8 % (7/90)	11.1 % (4/36)	5.4 % (2/37)	5.9 % (1/17)	0.62715
Other	1.1 % (1/90)	2.8 % (1/36)	0.0 % (0/37)	0.0 % (0/17)	0.46840
Glinide	3.5 % (287/8311)	3.0 % (97/3242)	3.6 % (101/2806)	3.9 % (89/2263)	0.14882
Glinide, dosage [mg/day]	14.34 ± 56.56, n=287	25.80 ± 80.55, n=97	3.49 ± 2.94, n=101	14.14 ± 55.05, n=89	0.18032
Substance					
Nateglinide	2.8 % (8/287)	5.2 % (5/97)	0.0 % (0/101)	3.4 % (3/89)	0.08152
Repaglinide	94.1 % (270/287)	91.8 % (89/97)	98.0 % (99/101)	92.1 % (82/89)	0.11301
Other	3.1 % (9/287)	3.1 % (3/97)	2.0 % (2/101)	4.5 % (4/89)	0.61097
Glitazone	0.5 % (43/8321)	0.6 % (18/3253)	0.5 % (14/2806)	0.5 % (11/2262)	0.93107

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
Glitazone, dosage [mg/day]	38.00 ± 22.38, n=42	35.56 ± 22.02, n=18	38.08 ± 11.64, n=13	41.91 ± 32.22, n=11	0.85634
Substance					
Pioglitazon	88.1 % (37/42)	94.4 % (17/18)	100.0 % (13/13)	63.6 % (7/11)	0.01276
Other	11.9 % (5/42)	5.6 % (1/18)	0.0 % (0/13)	36.4 % (4/11)	0.01276
DPP-4 inhibitors	62.5 % (5196/8311)	61.0 % (1975/3240)	64.1 % (1801/2808)	62.7 % (1420/2263)	0.03750
DPP-4 inhibitors, dosage [mg/day]	84.81 ± 33.05, n=5193	86.10 ± 31.36, n=1973	84.39 ± 36.68, n=1800	83.56 ± 30.34, n=1420	0.08040
Substance					
Sitagliptin	28.4 % (1476/5195)	28.9 % (571/1974)	27.7 % (498/1801)	28.7 % (407/1420)	0.66616
Vildagliptin	66.9 % (3477/5195)	67.6 % (1334/1974)	66.5 % (1198/1801)	66.5 % (945/1420)	0.73868
Linagliptin	0.0 % (1/5195)	0.0 % (0/1974)	0.1 % (1/1801)	0.0 % (0/1420)	0.38968
Saxagliptin	4.3 % (221/5195)	3.2 % (63/1974)	5.4 % (97/1801)	4.3 % (61/1420)	0.00381
Other	0.4 % (20/5195)	0.3 % (6/1974)	0.4 % (7/1801)	0.5 % (7/1420)	0.68035
GLP-1 analogs/mimetics	4.9 % (404/8326)	4.9 % (159/3255)	5.2 % (147/2809)	4.3 % (98/2262)	0.33053
GLP-1 analogs/mimetics, dosage [mg/day]	6.27 ± 12.93, n=401	5.66 ± 10.74, n=158	5.17 ± 13.21, n=147	8.95 ± 15.33, n=96	0.01919
Substance					
Exenatide	43.9 % (177/403)	43.4 % (69/159)	38.1 % (56/147)	53.6 % (52/97)	0.05672
Liraglutide	50.4 % (203/403)	49.1 % (78/159)	55.8 % (82/147)	44.3 % (43/97)	0.19712
Other	5.7 % (23/403)	7.5 % (12/159)	6.1 % (9/147)	2.1 % (2/97)	0.17883
SGTL-2 inhibitors	1.8 % (146/8327)	1.7 % (54/3256)	1.8 % (51/2809)	1.8 % (41/2262)	0.86965
SGTL-2 inhibitors, dosage [mg/day]	13.65 ± 16.44, n=144	14.63 ± 18.58, n=54	12.20 ± 13.97, n=50	14.15 ± 16.51, n=40	0.35853
Substance					
Dapagliflozin	95.1 % (137/144)	96.3 % (52/54)	94.0 % (47/50)	95.0 % (38/40)	0.86144
Other	4.9 % (7/144)	3.7 % (2/54)	6.0 % (3/50)	5.0 % (2/40)	0.86144
Total number of oral antidiabetics	1.71 ± 0.70, n=8332	1.69 ± 0.68, n=3258	1.75 ± 0.70, n=2810	1.70 ± 0.71, n=2264	0.00589
Median	2.0 (1.0, 2.0)	2.0 (1.0, 2.0)	2.0 (1.0, 2.0)	2.0 (1.0, 2.0)	
RANGE	0.0 , 5.0	0.0 , 5.0	0.0 , 4.0	0.0 , 4.0	
None	3.9 % (325/8332)	3.9 % (127/3258)	3.4 % (95/2810)	4.5 % (103/2264)	0.10185
1 OAD	30.5 % (2541/8332)	31.3 % (1019/3258)	29.4 % (826/2810)	30.7 % (696/2264)	0.27133
2 OADs	56.1 % (4676/8332)	56.7 % (1846/3258)	56.3 % (1583/2810)	55.1 % (1247/2264)	0.48812
>= 3 OADs	9.5 % (790/8332)	8.2 % (266/3258)	10.9 % (306/2810)	9.6 % (218/2264)	0.00141

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
Insulin(rapid-acting or long-acting or Pre-mixed)	15.1 % (1286/8536)	13.0 % (430/3319)	17.9 % (511/2853)	14.6 % (345/2364)	<.00001
Rapid-acting insulin	4.3 % (356/8329)	4.3 % (140/3256)	4.1 % (116/2811)	4.4 % (100/2262)	0.87210
Human insulin	50.0 % (178/356)	52.9 % (74/140)	40.5 % (47/116)	57.0 % (57/100)	0.03708
Analogues	50.0 % (178/356)	47.1 % (66/140)	59.5 % (69/116)	43.0 % (43/100)	0.03708
Syringe	3.4 % (12/356)	2.9 % (4/140)	4.3 % (5/116)	3.0 % (3/100)	0.79057
Pen	96.6 % (344/356)	97.1 % (136/140)	95.7 % (111/116)	97.0 % (97/100)	0.79057
Pump	0.0 % (0/356)	0.0 % (0/140)	0.0 % (0/116)	0.0 % (0/100)	
Other	0.0 % (0/356)	0.0 % (0/140)	0.0 % (0/116)	0.0 % (0/100)	
U-40	22.3 % (79/354)	22.9 % (32/140)	28.1 % (32/114)	15.0 % (15/100)	0.07106
U-100	77.7 % (275/354)	77.1 % (108/140)	71.9 % (82/114)	85.0 % (85/100)	0.07106
1x insulin/day	7.9 % (28/356)	10.0 % (14/140)	5.2 % (6/116)	8.0 % (8/100)	0.35993
2x insulin/day	16.0 % (57/356)	15.7 % (22/140)	15.5 % (18/116)	17.0 % (17/100)	0.94984
3x insulin/day	74.4 % (265/356)	73.6 % (103/140)	76.7 % (89/116)	73.0 % (73/100)	0.78563
4x insulin/day	1.7 % (6/356)	0.7 % (1/140)	2.6 % (3/116)	2.0 % (2/100)	0.49051
Long-acting insulin	12.6 % (1053/8330)	11.0 % (359/3256)	15.3 % (429/2810)	11.7 % (265/2264)	<.00001
Human insulin	29.8 % (314/1053)	31.5 % (113/359)	24.2 % (104/429)	36.6 % (97/265)	0.00177
Analogues	70.2 % (739/1053)	68.5 % (246/359)	75.8 % (325/429)	63.4 % (168/265)	0.00177
Syringe	5.8 % (61/1053)	5.8 % (21/359)	4.0 % (17/429)	8.7 % (23/265)	0.03543
Pen	93.8 % (988/1053)	94.2 % (338/359)	95.6 % (410/429)	90.6 % (240/265)	0.02755
Pump	0.2 % (2/1053)	0.0 % (0/359)	0.2 % (1/429)	0.4 % (1/265)	0.54434
Other	0.2 % (2/1053)	0.0 % (0/359)	0.2 % (1/429)	0.4 % (1/265)	0.54434
U-40	16.3 % (170/1046)	18.9 % (68/359)	11.3 % (48/424)	20.5 % (54/263)	0.00149
U-100	83.7 % (876/1046)	81.1 % (291/359)	88.7 % (376/424)	79.5 % (209/263)	0.00149
1x insulin/day	88.1 % (928/1053)	87.5 % (314/359)	88.6 % (380/429)	88.3 % (234/265)	0.88626
2x insulin/day	10.2 % (107/1053)	10.9 % (39/359)	9.8 % (42/429)	9.8 % (26/265)	0.86321

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
3x insulin/day	1.6 % (17/1053)	1.4 % (5/359)	1.6 % (7/429)	1.9 % (5/265)	0.88886
4x insulin/day	0.1 % (1/1053)	0.3 % (1/359)	0.0 % (0/429)	0.0 % (0/265)	0.38003
Pre-mixed insulin	1.6 % (133/8329)	1.4 % (44/3256)	1.8 % (51/2810)	1.7 % (38/2263)	0.33335
Human insulin	56.4 % (75/133)	63.6 % (28/44)	58.8 % (30/51)	44.7 % (17/38)	0.20590
Analogues	43.6 % (58/133)	36.4 % (16/44)	41.2 % (21/51)	55.3 % (21/38)	0.20590
Syringe	4.5 % (6/133)	6.8 % (3/44)	3.9 % (2/51)	2.6 % (1/38)	0.63877
Pen	95.5 % (127/133)	93.2 % (41/44)	96.1 % (49/51)	97.4 % (37/38)	0.63877
Pump	0.0 % (0/133)	0.0 % (0/44)	0.0 % (0/51)	0.0 % (0/38)	
Other	0.0 % (0/133)	0.0 % (0/44)	0.0 % (0/51)	0.0 % (0/38)	
U-40	18.0 % (24/133)	25.0 % (11/44)	11.8 % (6/51)	18.4 % (7/38)	0.24623
U-100	82.0 % (109/133)	75.0 % (33/44)	88.2 % (45/51)	81.6 % (31/38)	0.24623
1x insulin/day	11.3 % (15/133)	11.4 % (5/44)	7.8 % (4/51)	15.8 % (6/38)	0.50293
2x insulin/day	83.5 % (111/133)	84.1 % (37/44)	86.3 % (44/51)	78.9 % (30/38)	0.64861
3x insulin/day	3.8 % (5/133)	4.5 % (2/44)	3.9 % (2/51)	2.6 % (1/38)	0.89923
4x insulin/day	1.5 % (2/133)	0.0 % (0/44)	2.0 % (1/51)	2.6 % (1/38)	0.58567
Fixed-dose combination metformin / DPP-4 inhibitor	73.7 % (3093/4199)	75.1 % (1222/1628)	73.0 % (1067/1461)	72.4 % (804/1110)	0.24575
Novartis drugs					
Vildagliptin / Metformin					
Eucreas	91.9 % (2053/2233)	92.4 % (805/871)	90.8 % (708/780)	92.8 % (540/582)	0.32062
Icandra	8.1 % (180/2233)	7.6 % (66/871)	9.2 % (72/780)	7.2 % (42/582)	0.32062
Vildagliptin					
Galvus	86.8 % (1080/1244)	85.1 % (394/463)	86.4 % (361/418)	89.5 % (325/363)	0.16457
Jalra	13.2 % (164/1244)	14.9 % (69/463)	13.6 % (57/418)	10.5 % (38/363)	0.16457
Nateglinide					
STARLIX	100.0 % (8/8)	100.0 % (5/5)		100.0 % (3/3)	
Other	0.0 % (0/8)	0.0 % (0/5)		0.0 % (0/3)	

Table 9-31. *Current anti-hypertensive therapy in the SBP treatment groups at baseline.*

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
No. of patients	8536 (100.0 %)	3319 (38.9 %)	2853 (33.4 %)	2364 (27.7 %)	
ACE inhibitors	52.4 % (4363/8320)	51.0 % (1662/3257)	53.2 % (1488/2799)	53.6 % (1213/2264)	0.11296
ACE inhibitors, dosage [mg/day]	10.50 ± 12.68, n=4351	10.10 ± 12.39, n=1650	10.26 ± 11.69, n=1488	11.32 ± 14.14, n=1213	0.00226
Substance					
Captopril	2.7 % (116/4358)	2.8 % (46/1657)	2.3 % (34/1488)	3.0 % (36/1213)	0.51230
Enalapril	17.7 % (770/4358)	18.1 % (300/1657)	17.3 % (258/1488)	17.5 % (212/1213)	0.83579
Lisinopril	11.5 % (500/4358)	11.2 % (185/1657)	11.8 % (175/1488)	11.5 % (140/1213)	0.86852
Ramipril	65.3 % (2847/4358)	65.5 % (1086/1657)	65.7 % (978/1488)	64.6 % (783/1213)	0.79436
Trandolapril	0.1 % (6/4358)	0.1 % (2/1657)	0.2 % (3/1488)	0.1 % (1/1213)	0.68855
Other	2.7 % (119/4358)	2.3 % (38/1657)	2.7 % (40/1488)	3.4 % (41/1213)	0.20916
Angiotensin receptor blocker (ARB)	27.3 % (2272/8314)	27.1 % (882/3251)	28.0 % (785/2799)	26.7 % (605/2264)	0.54664
ARB, dosage [mg/day]	115.37 ± 115.94, n=2269	119.94 ± 118.39, n=879	110.06 ± 114.04, n=785	115.63 ± 114.70, n=605	0.21121
Substance					
Candesartan	22.9 % (521/2272)	22.8 % (201/882)	23.8 % (187/785)	22.0 % (133/605)	0.71543
Irbesartan	5.7 % (129/2272)	5.8 % (51/882)	5.1 % (40/785)	6.3 % (38/605)	0.62941
Losartan	7.9 % (179/2272)	6.7 % (59/882)	8.5 % (67/785)	8.8 % (53/605)	0.24257
Valsartan	39.0 % (887/2272)	41.3 % (364/882)	37.2 % (292/785)	38.2 % (231/605)	0.20703
Other	24.5 % (556/2272)	23.5 % (207/882)	25.4 % (199/785)	24.8 % (150/605)	0.65667
Direct renin inhibitor	0.5 % (39/8312)	0.5 % (16/3249)	0.5 % (14/2799)	0.4 % (9/2264)	0.84189
Direct renin inhibitor, dosage [mg/day]	208.15 ± 93.96, n=39	188.56 ± 100.45, n=16	246.43 ± 74.59, n=14	183.44 ± 99.77, n=9	0.17454
Beta-blocker	46.6 % (3874/8320)	45.6 % (1485/3257)	47.8 % (1338/2799)	46.4 % (1051/2264)	0.22583
Beta-blocker, dosage [mg/day]	53.22 ± 61.41, n=3864	52.78 ± 61.70, n=1476	56.02 ± 61.72, n=1337	50.26 ± 60.51, n=1051	0.05935
Substance					
Metoprolol	45.2 % (1751/3872)	45.1 % (669/1483)	47.2 % (631/1338)	42.9 % (451/1051)	0.11644
Bisoprolol	40.2 % (1558/3872)	40.6 % (602/1483)	38.1 % (510/1338)	42.4 % (446/1051)	0.09570
Nebivolol	6.1 % (237/3872)	5.9 % (88/1483)	6.4 % (86/1338)	6.0 % (63/1051)	0.84432

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
Carvedilol	4.7 % (182/3872)	4.5 % (66/1483)	5.1 % (68/1338)	4.6 % (48/1051)	0.71035
Other	3.7 % (144/3872)	3.9 % (58/1483)	3.2 % (43/1338)	4.1 % (43/1051)	0.46919
Calcium channel blocker	27.0 % (2244/8311)	25.2 % (818/3250)	26.8 % (751/2798)	29.8 % (675/2263)	0.00063
Calcium channel blocker, dosage [mg/day]	17.45 ± 41.26, n=2239	14.33 ± 30.50, n=814	18.79 ± 45.84, n=751	19.73 ± 46.65, n=674	0.40647
Substance					
Amlodipine	75.3 % (1690/2243)	76.0 % (622/818)	76.8 % (577/751)	72.8 % (491/674)	0.18583
Nifedipine	2.7 % (60/2243)	2.0 % (16/818)	2.7 % (20/751)	3.6 % (24/674)	0.16072
Nisoldipine	0.0 % (1/2243)	0.0 % (0/818)	0.1 % (1/751)	0.0 % (0/674)	0.37017
Nimodipine	0.0 % (1/2243)	0.1 % (1/818)	0.0 % (0/751)	0.0 % (0/674)	0.41836
Diltiazem	0.6 % (13/2243)	0.5 % (4/818)	0.0 % (0/751)	1.3 % (9/674)	0.00374
Verapamil	3.2 % (72/2243)	2.4 % (20/818)	3.1 % (23/751)	4.3 % (29/674)	0.12348
Gallopamil	0.0 % (0/2243)	0.0 % (0/818)	0.0 % (0/751)	0.0 % (0/674)	
Felodipine	2.9 % (65/2243)	2.4 % (20/818)	3.3 % (25/751)	3.0 % (20/674)	0.57591
Nitrendipine	4.3 % (96/2243)	4.3 % (35/818)	5.3 % (40/751)	3.1 % (21/674)	0.12023
Lercanidipine	9.7 % (218/2243)	10.8 % (88/818)	7.6 % (57/751)	10.8 % (73/674)	0.05405
Nilvadipine	0.0 % (1/2243)	0.1 % (1/818)	0.0 % (0/751)	0.0 % (0/674)	0.41836
Manidipine	0.0 % (1/2243)	0.1 % (1/818)	0.0 % (0/751)	0.0 % (0/674)	0.41836
Isradipine	0.1 % (3/2243)	0.2 % (2/818)	0.1 % (1/751)	0.0 % (0/674)	0.43739
Other	1.0 % (22/2243)	1.0 % (8/818)	0.9 % (7/751)	1.0 % (7/674)	0.97943
Diuretic drugs	42.6 % (3542/8317)	40.4 % (1314/3254)	42.3 % (1185/2799)	46.1 % (1043/2264)	0.00014
Diuretic drugs, dosage [mg/day]	18.8 (12.5, 25.0)	20.0 (12.5, 25.0)	20.0 (12.5, 25.0)	15.0 (12.5, 25.0)	0.63001
Substance					
Furosemide	8.4 % (296/3542)	8.0 % (105/1314)	8.0 % (95/1185)	9.2 % (96/1043)	0.49994
Torasemide	22.8 % (808/3542)	22.0 % (289/1314)	23.1 % (274/1185)	23.5 % (245/1043)	0.65820
Bumetanide	0.0 % (1/3542)	0.0 % (0/1314)	0.1 % (1/1185)	0.0 % (0/1043)	0.36980
Etacrynic acid	0.0 % (1/3542)	0.0 % (0/1314)	0.1 % (1/1185)	0.0 % (0/1043)	0.36980
Piretanide	1.1 % (40/3542)	1.1 % (15/1314)	1.4 % (16/1185)	0.9 % (9/1043)	0.55359
Hydrochlorothiazide	68.9 % (2442/3542)	70.1 % (921/1314)	68.4 % (810/1185)	68.2 % (711/1043)	0.52388
Clopamid	0.2 % (8/3542)	0.3 % (4/1314)	0.0 % (0/1185)	0.4 % (4/1043)	0.12291
Other	8.2 % (291/3542)	8.5 % (112/1314)	8.8 % (104/1185)	7.2 % (75/1043)	0.34783

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
Other anti-hypertensive therapy	10.1 % (841/8300)	9.0 % (291/3240)	10.7 % (298/2798)	11.1 % (252/2262)	0.01775
Total number of antihyper. Drugs	2.06 ± 1.15, n=8321	1.99 ± 1.15, n=3258	2.09 ± 1.12, n=2799	2.14 ± 1.19, n=2264	<.00001
Median	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)	
RANGE	0.0 , 6.0	0.0 , 6.0	0.0 , 6.0	0.0 , 6.0	
N	8321[N]	3258[N]	2799[N]	2264[N]	
None	6.5 % (541/8321)	7.4 % (241/3258)	5.3 % (148/2799)	6.7 % (152/2264)	0.00360
1 AHD	28.9 % (2401/8321)	31.5 % (1026/3258)	27.8 % (779/2799)	26.3 % (596/2264)	0.00006
2 AHDs	29.5 % (2452/8321)	28.0 % (911/3258)	31.5 % (881/2799)	29.2 % (660/2264)	0.01061
3 AHDs	23.9 % (1991/8321)	23.0 % (748/3258)	24.9 % (696/2799)	24.2 % (547/2264)	0.21209
>=4 AHDs	11.2 % (936/8321)	10.2 % (332/3258)	10.5 % (295/2799)	13.6 % (309/2264)	0.00012
Fixed-dose combinations					
Fixed-dose combination ARB/calcium channel blocker/diuretic	70.9 % (444/626)	67.2 % (156/232)	73.3 % (148/202)	72.9 % (140/192)	0.29620
Fixed-dose combination ACE inhibitor/diuretic	50.4 % (908/1802)	50.2 % (322/641)	51.8 % (317/612)	49.0 % (269/549)	0.63236
Fixed-dose combination ARB/diuretic	65.3 % (604/925)	64.2 % (240/374)	64.4 % (195/303)	68.1 % (169/248)	0.54462
Fixed-dose combination ARB/calcium channel blocker	37.8 % (185/490)	35.4 % (68/192)	42.9 % (76/177)	33.9 % (41/121)	0.19777
Fixed-dose combination ACE inhibitor/calcium channel blocker	14.3 % (153/1070)	15.5 % (59/381)	12.8 % (44/343)	14.5 % (50/346)	0.59158
Fixed-dose combination direct renin inhibitor/diuretic	56.5 % (13/23)	37.5 % (3/8)	54.5 % (6/11)	100.0 % (4/4)	0.11811
Novartis drugs					
Valsartan / Hydrochlorothiazide					
CoDiovan	32.4 % (69/213)	37.2 % (35/94)	29.4 % (20/68)	27.5 % (14/51)	0.39641
Codiovan forte	14.1 % (30/213)	10.6 % (10/94)	17.6 % (12/68)	15.7 % (8/51)	0.41813
Cordinate plus	1.4 % (3/213)	2.1 % (2/94)	1.5 % (1/68)	0.0 % (0/51)	0.58257
Provas	0.5 % (1/213)	0.0 % (0/94)	1.5 % (1/68)	0.0 % (0/51)	0.34260
Provas comp	6.6 % (14/213)	7.4 % (7/94)	8.8 % (6/68)	2.0 % (1/51)	0.29457
Provas maxx	1.9 % (4/213)	3.2 % (3/94)	0.0 % (0/68)	2.0 % (1/51)	0.33562
Other	43.2 % (92/213)	39.4 % (37/94)	41.2 % (28/68)	52.9 % (27/51)	0.26578
Valsartan					
Cordinate	4.0 % (13/321)	2.9 % (4/138)	3.0 % (3/101)	7.3 % (6/82)	0.22022

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
Diovan	34.9 % (112/321)	34.8 % (48/138)	32.7 % (33/101)	37.8 % (31/82)	0.76879
Provas	7.2 % (23/321)	3.6 % (5/138)	5.9 % (6/101)	14.6 % (12/82)	0.00780
Other	53.9 % (173/321)	58.7 % (81/138)	58.4 % (59/101)	40.2 % (33/82)	0.01608
Valsartan / Amlodipine / Hydrochlorothiazide					
Exforge HCT	77.0 % (164/213)	81.2 % (69/85)	79.7 % (55/69)	67.8 % (40/59)	0.13914
Dafiro HCT	13.1 % (28/213)	11.8 % (10/85)	13.0 % (9/69)	15.3 % (9/59)	0.83013
Other	9.9 % (21/213)	7.1 % (6/85)	7.2 % (5/69)	16.9 % (10/59)	0.09940
Aliskiren					
Rasilez	96.2 % (25/26)	100.0 % (13/13)	100.0 % (8/8)	80.0 % (4/5)	0.11259
Other	3.8 % (1/26)	0.0 % (0/13)	0.0 % (0/8)	20.0 % (1/5)	0.11259
Hydrochlorothiazide					
Esidrix	3.8 % (23/604)	5.7 % (14/244)	2.2 % (4/181)	2.8 % (5/179)	0.11970
Other	96.2 % (581/604)	94.3 % (230/244)	97.8 % (177/181)	97.2 % (174/179)	0.11970
Aliskiren / Hydrochlorothiazide					
Rasilez HCT	92.3 % (12/13)	66.7 % (2/3)	100.0 % (6/6)	100.0 % (4/4)	0.16438
Other	7.7 % (1/13)	33.3 % (1/3)	0.0 % (0/6)	0.0 % (0/4)	0.16438
Valsartan / Amlodipine					
Exforge	79.2 % (84/106)	73.7 % (28/38)	84.4 % (38/45)	78.3 % (18/23)	0.48007
Dafiro	16.0 % (17/106)	18.4 % (7/38)	15.6 % (7/45)	13.0 % (3/23)	0.85163
Other	4.7 % (5/106)	7.9 % (3/38)	0.0 % (0/45)	8.7 % (2/23)	0.14287

Table 9-32. *Hypoglycemic events in the SBP treatment groups before baseline*

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
No. of patients	8536 (100.0 %)	3319 (38.9 %)	2853 (33.4 %)	2364 (27.7 %)	
Hypoglycemic events within last 12 months					
Without specific symptoms	3.5 % (281/8065)	2.7 % (85/3177)	3.6 % (99/2721)	4.5 % (97/2167)	0.00174
No. of events	3.65 ± 4.63, n=276	4.04 ± 5.71, n=85	3.91 ± 4.85, n=97	3.03 ± 3.04, n=94	0.08883
Symptomatic, but controllable without external help	3.8 % (312/8151)	2.7 % (87/3208)	4.3 % (118/2747)	4.9 % (107/2196)	0.00008
No. of events	3.78 ± 4.62, n=306	2.99 ± 2.25, n=86	4.09 ± 5.35, n=116	4.11 ± 5.12, n=104	0.20917
External help needed	0.7 % (54/8171)	0.2 % (6/3212)	0.8 % (21/2752)	1.2 % (27/2207)	0.00002
No. of events	2.81 ± 2.50, n=54	3.17 ± 2.32, n=6	3.00 ± 2.61, n=21	2.59 ± 2.53, n=27	0.46496
Symptomatic with medical help	0.7 % (55/8180)	0.4 % (13/3211)	0.7 % (20/2754)	1.0 % (22/2215)	0.03058
No. of events	4.04 ± 2.83, n=55	2.85 ± 1.41, n=13	4.55 ± 3.86, n=20	4.27 ± 2.21, n=22	0.22153
Hospitalization required	0.2 % (13/8226)	0.2 % (5/3232)	0.3 % (8/2773)	0.0 % (0/2221)	0.03860
No. of events	1.08 ± 0.28, n=13	1.00 ± 0.00, n=5	1.13 ± 0.35, n=8	, n=0	0.52709[U]

Table 9-33. *Patient reported outcomes regarding diabetes and hypertension in the SBP treatment groups at baseline.*

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
No. of patients	8536 (100.0 %)	3319 (38.9 %)	2853 (33.4 %)	2364 (27.7 %)	
Antidiabetic therapy: impact on weight					
No change in weight	65.0 % (3269/5031)	67.0 % (1315/1964)	62.2 % (1102/1773)	65.8 % (852/1294)	0.00671
Weight gain	24.5 % (1233/5031)	22.5 % (441/1964)	26.8 % (476/1773)	24.4 % (316/1294)	0.00773
Weight loss	10.5 % (529/5031)	10.6 % (208/1964)	11.0 % (195/1773)	9.7 % (126/1294)	0.52624
Symptoms of hypoglycemia under antidiabetic medication					
No symptoms of hypoglycemia	85.3 % (4271/5008)	86.1 % (1684/1956)	85.3 % (1505/1765)	84.1 % (1082/1287)	0.28215
Once/twice symptoms of hypoglycemia	12.9 % (644/5008)	12.0 % (235/1956)	12.7 % (225/1765)	14.3 % (184/1287)	0.16209
Weekly symptoms of hypoglycemia	1.9 % (93/5008)	1.9 % (37/1956)	2.0 % (35/1765)	1.6 % (21/1287)	0.76911
Continuity of antidiabetic medication within last 12 months					
Continuous antidiabetic medication	71.8 % (3539/4928)	73.8 % (1416/1918)	71.8 % (1250/1740)	68.7 % (873/1270)	0.00757
Non-continuous antidiabetic medication	28.2 % (1389/4928)	26.2 % (502/1918)	28.2 % (490/1740)	31.3 % (397/1270)	0.00757
Continuity of antihypertensive medication within last 12 months					
Continuous antihypertensive medication	83.2 % (4078/4899)	83.9 % (1601/1909)	84.2 % (1458/1732)	81.0 % (1019/1258)	0.04615
Non-continuous antihypertensive medication	16.8 % (821/4899)	16.1 % (308/1909)	15.8 % (274/1732)	19.0 % (239/1258)	0.04615
No. of tablets for diabetes and hypertension					
1 - 3 tablets	48.0 % (2406/5009)	50.8 % (992/1954)	44.8 % (794/1773)	48.4 % (620/1282)	0.00122
4 - 6 tablets	42.5 % (2128/5009)	40.2 % (785/1954)	44.9 % (796/1773)	42.7 % (547/1282)	0.01423
7 or more tablets	9.5 % (475/5009)	9.1 % (177/1954)	10.3 % (183/1773)	9.0 % (115/1282)	0.32380

Table 9-34. *Quality of Life data (EQ-5D) in the SBP treatment groups at baseline.*

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
No. of patients	8536 (100.0 %)	3319 (38.9 %)	2853 (33.4 %)	2364 (27.7 %)	
Mobility					
No problems	73.5 % (3694/5027)	78.2 % (1536/1965)	72.4 % (1277/1765)	67.9 % (881/1297)	<.00001
Some problems	26.2 % (1319/5027)	21.7 % (426/1965)	27.2 % (480/1765)	31.8 % (413/1297)	<.00001
Confined to bed	0.3 % (14/5027)	0.2 % (3/1965)	0.5 % (8/1765)	0.2 % (3/1297)	0.20544
Self-care					
No problems	90.1 % (4523/5022)	93.0 % (1823/1961)	89.7 % (1583/1764)	86.1 % (1117/1297)	<.00001
Some problems	9.2 % (464/5022)	6.6 % (130/1961)	9.2 % (163/1764)	13.2 % (171/1297)	<.00001
Unable	0.7 % (35/5022)	0.4 % (8/1961)	1.0 % (18/1764)	0.7 % (9/1297)	0.08073
Usual activities					
No problems	76.9 % (3866/5025)	83.3 % (1637/1965)	74.0 % (1304/1761)	71.2 % (925/1299)	<.00001
Some problems	21.9 % (1102/5025)	15.7 % (308/1965)	24.9 % (438/1761)	27.4 % (356/1299)	<.00001
Unable	1.1 % (57/5025)	1.0 % (20/1965)	1.1 % (19/1761)	1.4 % (18/1299)	0.60114
Pain/discomfort					
None	50.5 % (2533/5013)	57.3 % (1123/1959)	48.9 % (860/1760)	42.5 % (550/1294)	<.00001
Moderate	45.5 % (2282/5013)	39.2 % (767/1959)	47.4 % (835/1760)	52.6 % (680/1294)	<.00001
Extreme	3.9 % (198/5013)	3.5 % (69/1959)	3.7 % (65/1760)	4.9 % (64/1294)	0.09857
Anxiety/depression					
Not anxious or depressed	72.9 % (3660/5021)	76.3 % (1497/1962)	69.7 % (1234/1770)	72.1 % (929/1289)	0.00003
Moderately anxious or depressed	24.6 % (1233/5021)	20.9 % (411/1962)	28.0 % (495/1770)	25.4 % (327/1289)	<.00001
Extremely anxious or depressed	2.5 % (128/5021)	2.8 % (54/1962)	2.3 % (41/1770)	2.6 % (33/1289)	0.70028
Health state today	72.0 (60.0, 82.0)	75.0 (60.0, 87.0)	70.0 (60.0, 80.0)	70.0 (60.0, 80.0)	<.00001
EQoL-D5 score acc. to Greiner, 2004	0.88 ± 0.18, n=4955	0.89 ± 0.17, n=1936	0.88 ± 0.17, n=1744	0.85 ± 0.19, n=1275	<.00001

9.3.3 HbA1c targets within SBP treatment goals

Table 9-35 shows frequency distributions of HbA1c targets within SBP treatment goals.

Table 9-35. *Frequency distribution of HbA1c targets within SBP treatment goals.*

	SBP <= 130 Strict treatment target	**SBP >130 - <= 135** Medium treatm. target	**SBP >135 - <= 140** Loose treatm. target	**TOTAL**
HbA1c <= 6.5 Strict treatment target	70.2% (2339/3333)	18.1% (602/3333)	11.8% (392/3333)	39.1% (3333/8533)
HbA1c >6.5 - <=7 Medium treatm. target	20.0% (724/3620)	52.2% (1888/3620)	27.8% (1008/3620)	42.4% (3620/8533)
HbA1c >7 - <=7.5 Loose treatm. target	16.1% (255/1580)	23.0% (363/1580)	60.9% (962/1580)	18.5% (1580/8533)

9.4 Treatment Success over Time

The data evaluation was performed for the total population and the three treatment target groups based on

- Initial target HbA1c: ≤ 6.5% [strict] / >6.5 – 7.0% [medium] / >7.0 – ≤ 7.5% [loose]
- Initial target systolic BP: ≤ 130 mmHg [strict] / >130 – 135 mmHg [medium] / >135 – - ≤ 140 mmHg [loose]

at 6, 12, 24 months follow-up in comparison.

The complete descriptive statistical report regarding the comparison of the treatment target groups (HbA1c; SBP) is given in Appendix 6.

9.4.1 Treatment success in the HbA1c treatment target groups

9.4.1.1 HbA1c target achievement

Table 9-36 shows frequency distributions of HbA1c target achievement rates at 6, 12, and 24 months follow-up.

Table 9-36. *Frequency distributions of HbA1c target achievement rates at 6, 12, and 24 months of follow-up.*

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
No. of patients with 6M-FU data	7355 (100.0 %)	2886 (39.2 %)	3197 (43.5 %)	1272 (17.3 %)	
Target HbA1c met	49.6 % (3333/6724)	45.8 % (1202/2622)	51.4 % (1509/2934)	53.3 % (622/1168)	<.00001
No. of patients with 12M-FU data	6691 (100.0 %)	2644 (39.5 %)	2912 (43.5 %)	1135 (17.0 %)	
Target HbA1c met	53.1 % (3226/6075)	46.2 % (1092/2363)	56.8 % (1528/2691)	59.4 % (606/1021)	<.00001
No. of patients with 24M-FU data	4130 (100.0 %)	1671 (40.5 %)	1808 (43.8 %)	651 (15.8 %)	
Target HbA1c met	55.8 % (2112/3783)	46.0 % (690/1499)	61.5 % (1032/1679)	64.5 % (390/605)	<.00001

9.4.1.2 Patient characteristics

Patient characteristics at 6-month follow-up

Table 9-37 shows vital status and cause of death in the HbA1c treatment groups at 6-month follow-up.

Table 9-38 shows newly diagnosed diseases and other events in the HbA1c treatment groups at 6-month follow-up.

Table 9-39 shows absolute and relative changes in clinical parameters (i.e. SBP; DBP, Heart rate; Weight; BMI; Waist circumference) in the HbA1c treatment groups at 6-month follow-up.

Table 9-40 shows absolute and relative changes in laboratory values (i.e. Cholesterol; Glucose; Haemoglobin; Creatinine; Liver function) in the HbA1c treatment groups at 6-month follow-up.

Table 9-37. *Vital status and cause of death in the HbA1c treatment groups at 6-month follow-up*

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
No. of patients with FU data	7355 (100.0 %)	2886 (39.2 %)	3197 (43.5 %)	1272 (17.3 %)	
FU date missing	0.1 % (4/7355)	0.0 % (1/2886)	0.1 % (2/3197)	0.1 % (1/1272)	0.82552
Vital status missing	0.1 % (5/7355)	0.0 % (0/2886)	0.1 % (3/3197)	0.2 % (2/1272)	0.15187
No. of days until 6-month FU	184.0 (177.0, 196.0)	184.0 (176.0, 196.0)	184.0 (177.0, 196.0)	185.0 (178.0, 197.0)	0.02753
Mortality	0.2 % (13/7350)	0.2 % (7/2886)	0.1 % (4/3194)	0.2 % (2/1270)	0.54484
Sudden cardiac death	15.4 % (2/13)	14.3 % (1/7)	0.0 % (0/4)	50.0 % (1/2)	0.27600
Other cardiovascular causes	7.7 % (1/13)	14.3 % (1/7)	0.0 % (0/4)	0.0 % (0/2)	0.62858
Cancer	38.5 % (5/13)	57.1 % (4/7)	0.0 % (0/4)	50.0 % (1/2)	0.16165
Other	23.1 % (3/13)	14.3 % (1/7)	50.0 % (2/4)	0.0 % (0/2)	0.28110
Unknown	15.4 % (2/13)	0.0 % (0/7)	50.0 % (2/4)	0.0 % (0/2)	0.07001
No. of days until death	134.0 (86.5, 156.5)	142.0 (99.0, 170.0)	104.0 (39.5, 148.5)	116.5 (82.0, 151.0)	0.43460

Table 9-38. *Newly diagnosed diseases and other events in the HbA1c treatment groups at 6-month follow-up*

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
No. of patients with FU data	7355 (100.0 %)	2886 (39.2 %)	3197 (43.5 %)	1272 (17.3 %)	
Coronary Heart Disease	0.2 % (18/7315)	0.3 % (8/2863)	0.2 % (7/3187)	0.2 % (3/1265)	0.89379
Myocardial infarction	0.1 % (10/7315)	0.2 % (5/2863)	0.1 % (2/3187)	0.2 % (3/1265)	0.28459
PCI	0.2 % (17/7314)	0.2 % (7/2863)	0.2 % (5/3186)	0.4 % (5/1265)	0.32509
CABG	0.0 % (1/7315)	0.0 % (0/2863)	0.0 % (1/3187)	0.0 % (0/1265)	0.52324
Peripheral angioplasty	0.1 % (6/7315)	0.1 % (2/2863)	0.1 % (4/3187)	0.0 % (0/1265)	0.40141
Peripheral bypass surgery	0.0 % (2/7314)	0.0 % (0/2863)	0.0 % (1/3186)	0.1 % (1/1265)	0.36072
Stroke/TIA	0.2 % (16/7314)	0.3 % (8/2862)	0.2 % (6/3187)	0.2 % (2/1265)	0.65931
Heart Failure	0.3 % (21/7313)	0.1 % (3/2861)	0.4 % (13/3187)	0.4 % (5/1265)	0.06523
NYHA I	23.8 % (5/21)	33.3 % (1/3)	15.4 % (2/13)	40.0 % (2/5)	0.50129
NYHA II	33.3 % (7/21)	33.3 % (1/3)	38.5 % (5/13)	20.0 % (1/5)	0.75811
NYHA III	33.3 % (7/21)	33.3 % (1/3)	30.8 % (4/13)	40.0 % (2/5)	0.93311
NYHA IV	9.5 % (2/21)	0.0 % (0/3)	15.4 % (2/13)	0.0 % (0/5)	0.50653
Peripheral arterial occlusive disease	0.2 % (14/7314)	0.1 % (4/2862)	0.3 % (8/3187)	0.2 % (2/1265)	0.58690
Dyslipidemia	0.3 % (22/7313)	0.2 % (7/2862)	0.4 % (12/3187)	0.2 % (3/1264)	0.58256
Autonomous neuropathy	0.1 % (10/7313)	0.1 % (4/2861)	0.1 % (3/3187)	0.2 % (3/1265)	0.50669
Non-proliferative diabetic retinopathy	0.1 % (4/7329)	0.0 % (1/2877)	0.0 % (0/3187)	0.2 % (3/1265)	0.00792
Proliferative diabetic retinopathy / laser coagulation	0.0 % (2/7328)	0.1 % (2/2877)	0.0 % (0/3186)	0.0 % (0/1265)	0.21277
Diabetic macular edema	0.0 % (1/7328)	0.0 % (1/2877)	0.0 % (0/3187)	0.0 % (0/1264)	0.46132
Blindness	0.0 % (1/7328)	0.0 % (0/2876)	0.0 % (1/3187)	0.0 % (0/1265)	0.52217
Dialysis	0.0 % (2/7329)	0.1 % (2/2878)	0.0 % (0/3186)	0.0 % (0/1265)	0.21289
Amputation	0.1 % (4/7355)	0.0 % (0/2886)	0.1 % (3/3197)	0.1 % (1/1272)	0.26937
Foot	25.0 % (1/4)		33.3 % (1/3)	0.0 % (0/1)	0.50499
Toes	75.0 % (3/4)		66.7 % (2/3)	100.0 % (1/1)	0.50499
Upper extremities	0.0 % (0/4)		0.0 % (0/3)	0.0 % (0/1)	
Lower extremities	0.0 % (0/4)		0.0 % (0/3)	0.0 % (0/1)	
Rehospitalisation	3.2 % (233/7328)	3.1 % (89/2867)	3.0 % (96/3191)	3.8 % (48/1270)	0.39828
Reasons					

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
Cardiac	21.9 % (51/233)	18.0 % (16/89)	27.1 % (26/96)	18.8 % (9/48)	0.27417
Diabetes	4.7 % (11/233)	2.2 % (2/89)	4.2 % (4/96)	10.4 % (5/48)	0.09357
Other	73.4 % (171/233)	79.8 % (71/89)	69.8 % (67/96)	68.8 % (33/48)	0.22049
Unknown	1.3 % (3/233)	1.1 % (1/89)	0.0 % (0/96)	4.2 % (2/48)	0.11072
Duration [weeks]	1.0 (1.0, 2.0)	1.0 (1.0, 2.0)	1.0 (1.0, 2.0)	1.0 (1.0, 2.0)	0.05525
Rehabilitation measures	0.8 % (55/7310)	0.9 % (27/2866)	0.5 % (17/3184)	0.9 % (11/1260)	0.16028
Reasons					
Cardiac	9.1 % (5/55)	11.1 % (3/27)	5.9 % (1/17)	9.1 % (1/11)	0.84152
Diabetes	21.8 % (12/55)	29.6 % (8/27)	17.6 % (3/17)	9.1 % (1/11)	0.33558
Other	69.1 % (38/55)	59.3 % (16/27)	82.4 % (14/17)	72.7 % (8/11)	0.26050
Unknown	1.8 % (1/55)	0.0 % (0/27)	0.0 % (0/17)	9.1 % (1/11)	0.13041
As out-patient	36.4 % (20/55)	40.7 % (11/27)	29.4 % (5/17)	36.4 % (4/11)	0.74879
As in-patient	63.6 % (35/55)	59.3 % (16/27)	70.6 % (12/17)	63.6 % (7/11)	0.74879
Duration [weeks]	3.0 (3.0, 4.0)	3.0 (3.0, 4.0)	3.0 (3.0, 3.0)	3.0 (3.0, 3.0)	0.94381
General practitioner consultations	89.6 % (6565/7326)	88.3 % (2530/2864)	91.1 % (2908/3191)	88.7 % (1127/1271)	0.00086
No. of contacts	5.01 ± 4.34, n=6565	5.35 ± 4.88, n=2530	4.61 ± 3.79, n=2908	5.28 ± 4.32, n=1127	<.00001
Specialist physician consultations	54.2 % (3971/7325)	50.8 % (1455/2863)	56.8 % (1814/3191)	55.2 % (702/1271)	0.00001
No. of contacts	2.28 ± 2.23, n=3971	2.27 ± 1.83, n=1455	2.25 ± 2.54, n=1814	2.39 ± 2.10, n=702	0.00576

Table 9-39. *Absolute and relative changes in clinical parameters in the HbA1c treatment groups at 6-month follow-up.*

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
No. of patients with FU data	7355 (100.0 %)	2886 (39.2 %)	3197 (43.5 %)	1272 (17.3 %)	
Systolic blood pressure	135.87 ± 13.92, n=7332	135.43 ± 13.99, n=2879	135.96 ± 13.81, n=3189	136.67 ± 14.02, n=1264	0.00213
Absolute change [FU - BL]	-4.59 ± 16.00, n=7323	-4.20 ± 16.59, n=2878	-4.85 ± 15.62, n=3188	-4.85 ± 15.58, n=1257	0.15651
Relative change [(FU - BL)/BL]	-0.03 ± 0.11, n=7323	-0.02 ± 0.12, n=2878	-0.03 ± 0.11, n=3188	-0.03 ± 0.11, n=1257	0.17100
[SBP FU6 - target SBP]	1.41 ± 13.84, n=7303	3.32 ± 13.85, n=2870	0.53 ± 13.71, n=3184	-0.73 ± 13.61, n=1249	<.00001
Target SBP met	56.1 % (4116/7331)	51.2 % (1474/2879)	57.8 % (1843/3188)	63.2 % (799/1264)	<.00001
Diastolic blood pressure	80.57 ± 8.55, n=7332	80.86 ± 8.66, n=2879	80.36 ± 8.44, n=3189	80.41 ± 8.56, n=1264	0.15310
Absolute change [FU - BL]	-2.16 ± 9.90, n=7323	-1.68 ± 10.41, n=2878	-2.38 ± 9.69, n=3188	-2.70 ± 9.18, n=1257	0.00544
Relative change [(FU - BL)/BL]	-0.02 ± 0.13, n=7323	-0.01 ± 0.13, n=2878	-0.02 ± 0.12, n=3188	-0.03 ± 0.12, n=1257	0.00582
[DBP FU6 - target SBP]	-3.03 ± 8.92, n=7332	-0.85 ± 8.74, n=2879	-4.15 ± 8.75, n=3189	-5.17 ± 8.70, n=1264	<.00001
Target DBP met	76.0 % (5575/7331)	68.8 % (1981/2879)	79.4 % (2531/3188)	84.1 % (1063/1264)	<.00001
Heart rate [/min]	74.09 ± 9.36, n=7312	74.22 ± 9.63, n=2867	73.80 ± 8.90, n=3185	74.50 ± 9.86, n=1260	0.27784
Absolute change [FU - BL]	-0.99 ± 9.73, n=7296	-0.74 ± 10.18, n=2861	-1.15 ± 9.33, n=3182	-1.13 ± 9.65, n=1253	0.08848
Relative change [(FU - BL)/BL]	-0.00 ± 0.13, n=7296	0.00 ± 0.14, n=2861	-0.01 ± 0.12, n=3182	-0.01 ± 0.13, n=1253	0.09603
Weight [kg]	89.78 ± 18.47, n=7336	89.45 ± 18.56, n=2879	89.82 ± 18.29, n=3191	90.43 ± 18.71, n=1266	0.31793
Absolute change [FU - BL]	-0.68 ± 5.02, n=7334	-0.69 ± 5.23, n=2879	-0.64 ± 4.70, n=3191	-0.75 ± 5.30, n=1264	0.65484
Relative change [(FU - BL)/BL]	-0.01 ± 0.06, n=7334	-0.01 ± 0.06, n=2879	-0.01 ± 0.05, n=3191	-0.01 ± 0.06, n=1264	0.65151
BMI [kg/m2]	31.04 ± 5.87, n=7329	30.87 ± 5.89, n=2878	31.10 ± 5.80, n=3189	31.29 ± 5.97, n=1262	0.07930
Absolute change [FU - BL]	-0.23 ± 1.77, n=7329	-0.24 ± 1.82, n=2878	-0.21 ± 1.66, n=3189	-0.25 ± 1.90, n=1262	0.69709
Relative change [(FU - BL)/BL]	-0.01 ± 0.06, n=7329	-0.01 ± 0.06, n=2878	-0.01 ± 0.05, n=3189	-0.01 ± 0.06, n=1262	0.66021
BMI < 25	11.2 % (820/7329)	11.8 % (340/2878)	10.8 % (345/3189)	10.7 % (135/1262)	0.39097
BMI: 25 - 30	38.4 % (2815/7329)	39.0 % (1121/2878)	38.7 % (1233/3189)	36.5 % (461/1262)	0.31199

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
BMI > 30	50.4 % (3694/7329)	49.2 % (1417/2878)	50.5 % (1611/3189)	52.8 % (666/1262)	0.10958
Waist circumference [cm]	108.78 ± 18.05, n=2229	108.70 ± 18.33, n=879	108.48 ± 17.89, n=1050	110.03 ± 17.82, n=300	0.18452
Absolute change [FU - BL]	0.03 ± 10.28, n=1989	0.02 ± 9.96, n=788	0.07 ± 10.44, n=929	-0.05 ± 10.67, n=272	0.53411
Relative change [(FU - BL)/BL]	0.00 ± 0.10, n=1989	0.00 ± 0.09, n=788	0.00 ± 0.10, n=929	0.00 ± 0.10, n=272	0.47659
Diabetes training since baseline	24.7 % (1810/7323)	24.0 % (692/2878)	24.7 % (786/3187)	26.4 % (332/1258)	0.27262
Participation in DMP diabetes	83.7 % (6129/7323)	83.5 % (2404/2878)	84.0 % (2677/3187)	83.3 % (1048/1258)	0.81471

Table 9-40. *Absolute and relative changes in laboratory values in the HbA1c treatment groups at 6-month follow-up.*

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
No. of patients with FU data	7355 (100.0 %)	2886 (39.2 %)	3197 (43.5 %)	1272 (17.3 %)	
Total fasting cholesterol available	68.0 % (5002/7355)	66.4 % (1917/2886)	69.4 % (2218/3197)	68.2 % (867/1272)	0.04742
Total fasting cholesterol [mmol/L]	9.78 ± 3.21, n=5002	9.76 ± 3.22, n=1917	9.79 ± 3.16, n=2218	9.82 ± 3.30, n=867	0.99733
Absolute change [FU - BL]	4.45 ± 2.88, n=4675	4.46 ± 2.88, n=1782	4.49 ± 2.83, n=2077	4.31 ± 3.00, n=816	0.30537
Relative change [(FU - BL)/BL]	0.87 ± 0.55, n=4675	0.87 ± 0.56, n=1782	0.88 ± 0.54, n=2077	0.83 ± 0.57, n=816	0.04419
Fasting HDL-cholesterol available	56.3 % (4144/7355)	55.5 % (1601/2886)	58.1 % (1858/3197)	53.9 % (685/1272)	0.01671
Fasting HDL-cholesterol [mmol/L]	1.27 ± 0.37, n=4144	1.31 ± 0.39, n=1601	1.25 ± 0.36, n=1858	1.25 ± 0.36, n=685	<.00001
Absolute change [FU - BL]	0.01 ± 0.29, n=3724	0.01 ± 0.31, n=1434	0.02 ± 0.24, n=1664	0.00 ± 0.38, n=626	0.13946
Relative change [(FU - BL)/BL]	0.05 ± 0.80, n=3724	0.03 ± 0.24, n=1434	0.06 ± 1.17, n=1664	0.03 ± 0.18, n=626	0.10234
Fasting LDL-cholesterol available	55.8 % (4103/7355)	54.5 % (1574/2886)	57.4 % (1834/3197)	54.6 % (695/1272)	0.05684
Fasting LDL-cholesterol [mmol/L]	3.09 ± 0.95, n=4103	3.09 ± 0.94, n=1574	3.07 ± 0.96, n=1834	3.13 ± 0.98, n=695	0.53738
Absolute change [FU - BL]	-0.12 ± 0.76, n=3685	-0.08 ± 0.77, n=1411	-0.14 ± 0.75, n=1640	-0.15 ± 0.78, n=634	0.01474
Relative change [(FU - BL)/BL]	0.06 ± 1.67, n=3685	0.08 ± 1.60, n=1411	0.07 ± 1.99, n=1640	0.01 ± 0.57, n=634	0.01821
Fasting triglycerides available	59.6 % (4383/7355)	59.2 % (1709/2886)	61.4 % (1964/3197)	55.8 % (710/1272)	0.00225
Fasting triglycerides [mmol/L]	2.11 ± 1.29, n=4383	2.05 ± 1.15, n=1709	2.11 ± 1.30, n=1964	2.24 ± 1.56, n=710	0.10725
Absolute change [FU - BL]	-0.19 ± 1.16, n=3987	-0.14 ± 1.08, n=1543	-0.17 ± 1.08, n=1792	-0.36 ± 1.50, n=652	0.00248
Relative change [(FU - BL)/BL]	0.05 ± 1.51, n=3987	0.06 ± 0.76, n=1543	0.04 ± 1.48, n=1792	0.05 ± 2.54, n=652	0.00422
Fasting glucose available	72.8 % (5355/7355)	72.5 % (2093/2886)	74.2 % (2372/3197)	70.0 % (890/1272)	0.01497
Fasting glucose [mmol/L]	7.42 ± 2.15, n=5355	7.01 ± 1.97, n=2093	7.43 ± 1.92, n=2372	8.37 ± 2.75, n=890	<.00001
Absolute change [FU - BL]	-1.04 ± 2.67, n=5077	-0.69 ± 2.40, n=1986	-1.24 ± 2.63, n=2263	-1.36 ± 3.27, n=828	<.00001
Relative change [(FU - BL)/BL]	-0.07 ± 0.44, n=5077	-0.04 ± 0.28, n=1986	-0.09 ± 0.57, n=2263	-0.09 ± 0.33, n=828	<.00001
Postprandial glucose available	39.2 % (2882/7355)	35.6 % (1028/2886)	42.6 % (1363/3197)	38.6 % (491/1272)	<.00001

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
Postprandial glucose [mmol/L]	8.88 ± 2.77, n=2882	8.48 ± 2.55, n=1028	8.85 ± 2.75, n=1363	9.80 ± 3.08, n=491	<.00001
Absolute change [FU - BL]	-1.87 ± 3.30, n=2418	-1.30 ± 3.10, n=866	-2.19 ± 3.27, n=1139	-2.16 ± 3.60, n=413	<.00001
Relative change [(FU - BL)/BL]	-0.07 ± 1.09, n=2418	-0.01 ± 1.30, n=866	-0.11 ± 1.03, n=1139	-0.11 ± 0.66, n=413	<.00001
HbA1c [%]	7.11 ± 1.04, n=6724	6.79 ± 0.94, n=2622	7.16 ± 0.93, n=2934	7.69 ± 1.20, n=1168	<.00001
[HbA1c FU6 - target HbA1c]	0.21 ± 0.99, n=6724	0.29 ± 0.94, n=2622	0.16 ± 0.93, n=2934	0.19 ± 1.20, n=1168	<.00001
Target HbA1c met	49.6 % (3333/6724)	45.8 % (1202/2622)	51.4 % (1509/2934)	53.3 % (622/1168)	<.00001
Absolute change [FU - BL]	-0.66 ± 1.27, n=6523	-0.46 ± 1.18, n=2537	-0.73 ± 1.24, n=2852	-0.94 ± 1.47, n=1134	<.00001
Relative change [(FU - BL)/BL]	-0.07 ± 0.13, n=6523	-0.05 ± 0.13, n=2537	-0.08 ± 0.13, n=2852	-0.10 ± 0.14, n=1134	<.00001
Haemoglobin available	48.1 % (3540/7355)	43.3 % (1249/2886)	51.9 % (1660/3197)	49.6 % (631/1272)	<.00001
Haemoglobin [mmol/L]	8.36 ± 1.34, n=3540	8.33 ± 1.33, n=1249	8.38 ± 1.36, n=1660	8.35 ± 1.33, n=631	0.40131
Absolute change [FU - BL]	-0.01 ± 0.69, n=3066	0.03 ± 0.82, n=1056	-0.02 ± 0.60, n=1452	-0.03 ± 0.66, n=558	0.90614
Relative change [(FU - BL)/BL]	0.00 ± 0.11, n=3066	0.01 ± 0.13, n=1056	0.00 ± 0.10, n=1452	-0.00 ± 0.09, n=558	0.94149
Serum creatinine available	72.2 % (5313/7355)	72.5 % (2093/2886)	72.6 % (2320/3197)	70.8 % (900/1272)	0.43052
Serum creatinine [µmol/l]	83.69 ± 37.80, n=5313	82.59 ± 28.26, n=2093	84.48 ± 48.14, n=2320	84.23 ± 24.50, n=900	0.04634
Absolute change [FU - BL]	-1.65 ± 58.45, n=4856	-3.09 ± 62.27, n=1887	-0.20 ± 51.78, n=2137	-2.10 ± 65.22, n=832	0.13303
Relative change [(FU - BL)/BL]	0.02 ± 0.36, n=4856	0.02 ± 0.24, n=1887	0.02 ± 0.49, n=2137	0.02 ± 0.18, n=832	0.08573
Microalbustix albumin [mg/l]	19.86 ± 33.57, n=1615	20.59 ± 32.49, n=531	20.46 ± 34.77, n=815	16.60 ± 31.88, n=269	0.00388
Microalbustix creatinine [mg/dl]	38.15 ± 73.37, n=908	56.91 ± 87.19, n=284	32.50 ± 68.20, n=443	22.54 ± 53.58, n=181	<.00001
Macroalbuminuria: positive test	6.8 % (264/3903)	5.8 % (83/1432)	7.1 % (125/1771)	8.0 % (56/700)	0.13094
Macroalbuminuria: negative test	93.2 % (3639/3903)	94.2 % (1349/1432)	92.9 % (1646/1771)	92.0 % (644/700)	0.13094
Increased liver function readings	12.1 % (516/4248)	11.7 % (188/1611)	11.5 % (216/1878)	14.8 % (112/759)	0.05184

Patient characteristics at 12-month follow-up

Table 9-41 shows vital status and cause of death in the HbA1c treatment groups at 12-month follow-up.

Table 9-42 shows newly diagnosed diseases and other events in the HbA1c treatment groups at 12-month follow-up.

Table 9-43 shows absolute and relative changes in clinical parameters (i.e. SBP; DBP, Heart rate; Weight; BMI; Waist circumference) in the HbA1c treatment groups at 12-month follow-up.

Table 9-44 shows absolute and relative changes in laboratory values (i.e. Cholesterol; Glucose; Haemoglobin; Creatinine; Liver function) in the HbA1c treatment groups at 12-month follow-up.

Table 9-41. *Vital status and cause of death in the HbA1c treatment groups at 12-month follow-up*

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
No. of patients with FU data	6691 (100.0 %)	2644 (39.5 %)	2912 (43.5 %)	1135 (17.0 %)	
FU date missing	0.1 % (5/6691)	0.0 % (0/2644)	0.0 % (1/2912)	0.4 % (4/1135)	0.00077
Vital status missing	0.1 % (7/6691)	0.1 % (2/2644)	0.1 % (2/2912)	0.3 % (3/1135)	0.18805
No. of days until 12-month FU	367.0 (361.0, 380.0)	367.0 (360.0, 380.0)	367.0 (361.0, 379.0)	368.0 (362.0, 380.0)	0.25327
Cumulative 1-year Mortality	0.3 % (23/8567)	0.3 % (11/3342)	0.2 % (8/3625)	0.3 % (4/1600)	0.67403
Sudden cardiac death	17.4 % (4/23)	18.2 % (2/11)	0.0 % (0/8)	50.0 % (2/4)	0.09781
Other cardiovascular causes	13.0 % (3/23)	9.1 % (1/11)	12.5 % (1/8)	25.0 % (1/4)	0.71973
Cancer	26.1 % (6/23)	36.4 % (4/11)	12.5 % (1/8)	25.0 % (1/4)	0.50387
Other	26.1 % (6/23)	18.2 % (2/11)	50.0 % (4/8)	0.0 % (0/4)	0.12613
Unknown	17.4 % (4/23)	18.2 % (2/11)	25.0 % (2/8)	0.0 % (0/4)	0.55731
No. of days until death	193.0 (131.0, 254.0)	193.0 (131.0, 246.0)	207.0 (104.0, 266.5)	187.0 (116.5, 224.0)	0.81167

Table 9-42. *Newly diagnosed diseases and other events in the HbA1c treatment groups at 12-month follow-up.*

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
No. of patients with FU data	6691 (100.0 %)	2644 (39.5 %)	2912 (43.5 %)	1135 (17.0 %)	
Coronary Heart Disease	0.3 % (18/6675)	0.3 % (9/2642)	0.3 % (8/2905)	0.1 % (1/1128)	0.39203
Myocardial infarction	0.1 % (9/6675)	0.2 % (4/2642)	0.1 % (4/2905)	0.1 % (1/1128)	0.88946
PCI	0.1 % (8/6675)	0.1 % (2/2642)	0.2 % (5/2905)	0.1 % (1/1128)	0.55298
CABG	0.1 % (10/6675)	0.1 % (3/2642)	0.2 % (7/2905)	0.0 % (0/1128)	0.17049
Peripheral angioplasty	0.1 % (5/6674)	0.1 % (3/2642)	0.0 % (1/2905)	0.1 % (1/1127)	0.55107
Peripheral bypass surgery	0.0 % (1/6675)	0.0 % (1/2642)	0.0 % (0/2905)	0.0 % (0/1128)	0.46610
Stroke/TIA	0.1 % (10/6675)	0.0 % (1/2642)	0.3 % (8/2905)	0.1 % (1/1128)	0.06209
Heart Failure	0.3 % (18/6676)	0.1 % (3/2642)	0.3 % (10/2906)	0.4 % (5/1128)	0.11897
NYHA I	11.1 % (2/18)	0.0 % (0/3)	10.0 % (1/10)	20.0 % (1/5)	0.67452
NYHA II	16.7 % (3/18)	0.0 % (0/3)	20.0 % (2/10)	20.0 % (1/5)	0.69768
NYHA III	61.1 % (11/18)	66.7 % (2/3)	60.0 % (6/10)	60.0 % (3/5)	0.97689
NYHA IV	11.1 % (2/18)	33.3 % (1/3)	10.0 % (1/10)	0.0 % (0/5)	0.34344
Peripheral arterial occlusive disease	0.2 % (14/6674)	0.2 % (4/2641)	0.2 % (6/2905)	0.4 % (4/1128)	0.45820
Dyslipidemia	0.2 % (13/6675)	0.2 % (4/2642)	0.2 % (7/2905)	0.2 % (2/1128)	0.74369
Autonomous neuropathy	0.1 % (6/6674)	0.0 % (1/2641)	0.2 % (5/2905)	0.0 % (0/1128)	0.13551
Non-proliferative diabetic retinopathy	0.0 % (0/6674)	0.0 % (0/2641)	0.0 % (0/2905)	0.0 % (0/1128)	
Proliferative diabetic retinopathy / laser coagulation	0.0 % (2/6674)	0.0 % (0/2641)	0.0 % (1/2905)	0.1 % (1/1128)	0.34860
Diabetic macular edema	0.0 % (2/6674)	0.0 % (1/2641)	0.0 % (0/2905)	0.1 % (1/1128)	0.32914
Blindness	0.0 % (0/6674)	0.0 % (0/2641)	0.0 % (0/2905)	0.0 % (0/1128)	
Dialysis	0.0 % (2/6674)	0.0 % (0/2641)	0.1 % (2/2905)	0.0 % (0/1128)	0.27313
Amputation	0.0 % (0/6691)	0.0 % (0/2644)	0.0 % (0/2912)	0.0 % (0/1135)	
Foot					
Toes					
Upper extremities					
Lower extremities					
Rehospitalisation	2.5 % (167/6677)	2.2 % (59/2642)	2.6 % (77/2907)	2.7 % (31/1128)	0.51677
Reasons					
Cardiac	35.3 % (59/167)	32.2 % (19/59)	33.8 % (26/77)	45.2 % (14/31)	0.43905

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
Diabetes	3.0 % (5/167)	3.4 % (2/59)	0.0 % (0/77)	9.7 % (3/31)	0.02765
Other	62.9 % (105/167)	66.1 % (39/59)	67.5 % (52/77)	45.2 % (14/31)	0.07631
Unknown	0.6 % (1/167)	1.7 % (1/59)	0.0 % (0/77)	0.0 % (0/31)	0.39821
Duration [weeks]	1.0 (1.0, 2.0)	1.0 (1.0, 2.0)	1.0 (1.0, 2.0)	1.0 (1.0, 2.0)	0.98000
Rehabilitation measures	0.7 % (46/6675)	0.6 % (17/2643)	0.8 % (24/2904)	0.4 % (5/1128)	0.39104
Reasons					
Cardiac	37.0 % (17/46)	29.4 % (5/17)	41.7 % (10/24)	40.0 % (2/5)	0.71758
Diabetes	6.5 % (3/46)	11.8 % (2/17)	4.2 % (1/24)	0.0 % (0/5)	0.51332
Other	56.5 % (26/46)	64.7 % (11/17)	50.0 % (12/24)	60.0 % (3/5)	0.63656
Unknown	2.2 % (1/46)	0.0 % (0/17)	4.2 % (1/24)	0.0 % (0/5)	0.62593
As out-patient	10.9 % (5/46)	11.8 % (2/17)	12.5 % (3/24)	0.0 % (0/5)	0.70834
As in-patient	89.1 % (41/46)	88.2 % (15/17)	87.5 % (21/24)	100.0 % (5/5)	0.70834
Duration [weeks]	3.0 (3.0, 4.0)	3.0 (3.0, 4.0)	3.0 (3.0, 3.5)	3.0 (3.0, 3.0)	0.99379
General practitioner consultations	90.4 % (6038/6676)	88.5 % (2339/2643)	91.8 % (2667/2905)	91.5 % (1032/1128)	0.00007
No. of contacts	4.0 (2.0, 6.0)	4.0 (2.0, 6.0)	3.0 (2.0, 6.0)	4.0 (2.0, 6.0)	0.00543
Specialist physician consultations	56.3 % (3759/6676)	50.9 % (1345/2643)	60.3 % (1753/2905)	58.6 % (661/1128)	<.00001
No. of contacts	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)	2.0 (1.0, 2.0)	2.0 (1.0, 3.0)	0.18480

Table 9-43. *Absolute and relative changes in clinical parameters in the HbA1c treatment groups at 12-month follow-up.*

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
No. of patients with FU data	6691 (100.0 %)	2644 (39.5 %)	2912 (43.5 %)	1135 (17.0 %)	
Systolic blood pressure	135.38 ± 13.48, n=6669	134.91 ± 13.25, n=2640	135.38 ± 13.57, n=2903	136.52 ± 13.72, n=1126	0.00172
Absolute change [FU - BL]	-4.93 ± 16.51, n=6663	-4.66 ± 16.85, n=2639	-5.16 ± 16.25, n=2902	-5.00 ± 16.36, n=1122	0.08409
Relative change [(FU - BL)/BL]	-0.03 ± 0.11, n=6663	-0.02 ± 0.12, n=2639	-0.03 ± 0.11, n=2902	-0.03 ± 0.11, n=1122	0.06633
[SBP FU12 - target SBP]	1.04 ± 13.52, n=6643	2.93 ± 13.08, n=2631	0.05 ± 13.68, n=2898	-0.86 ± 13.61, n=1114	<.00001
Target SBP met	57.0 % (3804/6668)	50.8 % (1341/2640)	60.0 % (1740/2902)	64.2 % (723/1126)	<.00001
Diastolic blood pressure	80.33 ± 8.13, n=6669	80.20 ± 8.26, n=2640	80.30 ± 8.04, n=2903	80.71 ± 8.04, n=1126	0.07993
Absolute change [FU - BL]	-2.46 ± 10.04, n=6663	-2.42 ± 10.41, n=2639	-2.43 ± 9.75, n=2902	-2.64 ± 9.90, n=1122	0.68449
Relative change [(FU - BL)/BL]	-0.02 ± 0.13, n=6663	-0.02 ± 0.13, n=2639	-0.02 ± 0.12, n=2902	-0.02 ± 0.13, n=1122	0.74534
[DBP FU12 - target SBP]	-3.21 ± 8.57, n=6669	-1.45 ± 8.40, n=2640	-4.15 ± 8.50, n=2903	-4.91 ± 8.46, n=1126	<.00001
Target DBP met	77.1 % (5140/6668)	71.4 % (1885/2640)	79.8 % (2317/2902)	83.3 % (938/1126)	<.00001
Heart rate [/min]	73.81 ± 9.00, n=6651	74.02 ± 9.07, n=2631	73.48 ± 8.78, n=2895	74.18 ± 9.39, n=1125	0.04222
Absolute change [FU - BL]	-1.33 ± 10.56, n=6636	-1.07 ± 10.75, n=2622	-1.48 ± 10.18, n=2893	-1.52 ± 11.04, n=1121	0.01245
Relative change [(FU - BL)/BL]	-0.01 ± 0.14, n=6636	-0.00 ± 0.14, n=2622	-0.01 ± 0.14, n=2893	-0.01 ± 0.15, n=1121	0.00879
Weight [kg]	89.42 ± 18.27, n=6669	89.39 ± 18.37, n=2640	89.16 ± 18.08, n=2903	90.17 ± 18.51, n=1126	0.28249
Absolute change [FU - BL]	-0.97 ± 5.63, n=6668	-0.81 ± 5.82, n=2640	-1.15 ± 5.59, n=2903	-0.90 ± 5.27, n=1125	0.04194
Relative change [(FU - BL)/BL]	-0.01 ± 0.06, n=6668	-0.01 ± 0.07, n=2640	-0.01 ± 0.06, n=2903	-0.01 ± 0.06, n=1125	0.04887
BMI [kg/m2]	30.92 ± 5.77, n=6665	30.84 ± 5.81, n=2640	30.89 ± 5.70, n=2902	31.21 ± 5.83, n=1123	0.13909
Absolute change [FU - BL]	-0.33 ± 1.94, n=6665	-0.28 ± 2.03, n=2640	-0.39 ± 1.90, n=2902	-0.30 ± 1.85, n=1123	0.04673
Relative change [(FU - BL)/BL]	-0.01 ± 0.06, n=6665	-0.01 ± 0.07, n=2640	-0.01 ± 0.06, n=2902	-0.01 ± 0.06, n=1123	0.05074
BMI < 25	11.8 % (789/6665)	12.3 % (325/2640)	11.7 % (339/2902)	11.1 % (125/1123)	0.55682
BMI: 25 - 30	38.0 % (2531/6665)	38.8 % (1023/2640)	38.2 % (1110/2902)	35.4 % (398/1123)	0.14749

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
BMI > 30	50.2 % (3345/6665)	48.9 % (1292/2640)	50.1 % (1453/2902)	53.4 % (600/1123)	0.04119
Waist circumference [cm]	107.02 ± 15.25, n=1842	107.22 ± 15.76, n=739	106.38 ± 14.55, n=870	108.80 ± 16.09, n=233	0.07805
Absolute change [FU - BL]	-1.10 ± 7.61, n=1626	-0.94 ± 8.29, n=653	-1.32 ± 5.73, n=767	-0.80 ± 10.85, n=206	0.52764
Relative change [(FU - BL)/BL]	-0.01 ± 0.07, n=1626	-0.01 ± 0.09, n=653	-0.01 ± 0.05, n=767	-0.00 ± 0.10, n=206	0.49700
Diabetes training FU12	32.6 % (2172/6671)	34.9 % (921/2640)	29.9 % (868/2903)	34.0 % (383/1128)	0.00022
Participation in DMP diabetes	83.1 % (5546/6671)	83.3 % (2198/2640)	83.6 % (2428/2903)	81.6 % (920/1128)	0.27993

Table 9-44. *Absolute and relative changes in laboratory values in the HbA1c treatment groups at 12-month follow-up.*

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
No. of patients with FU data	6691 (100.0 %)	2644 (39.5 %)	2912 (43.5 %)	1135 (17.0 %)	
Total fasting cholesterol available	67.0 % (4481/6691)	63.5 % (1680/2644)	69.5 % (2023/2912)	68.5 % (778/1135)	<.00001
Total fasting cholesterol [mmol/L]	9.68 ± 3.23, n=4481	9.69 ± 3.28, n=1680	9.71 ± 3.15, n=2023	9.56 ± 3.31, n=778	0.60502
Absolute change [FU - BL]	4.33 ± 2.95, n=4240	4.40 ± 2.93, n=1584	4.37 ± 2.89, n=1917	4.08 ± 3.14, n=739	0.10229
Relative change [(FU - BL)/BL]	0.85 ± 0.57, n=4240	0.87 ± 0.58, n=1584	0.86 ± 0.55, n=1917	0.79 ± 0.61, n=739	0.00316
Fasting HDL-cholesterol available	53.9 % (3605/6691)	51.2 % (1354/2644)	55.4 % (1614/2912)	56.1 % (637/1135)	0.00176
Fasting HDL-cholesterol [mmol/L]	1.28 ± 0.37, n=3605	1.32 ± 0.38, n=1354	1.26 ± 0.35, n=1614	1.27 ± 0.36, n=637	0.00006
Absolute change [FU - BL]	0.03 ± 0.32, n=3300	0.03 ± 0.33, n=1234	0.03 ± 0.26, n=1482	0.01 ± 0.40, n=584	0.11534
Relative change [(FU - BL)/BL]	0.05 ± 0.31, n=3300	0.05 ± 0.26, n=1234	0.05 ± 0.31, n=1482	0.05 ± 0.38, n=584	0.09029
Fasting LDL-cholesterol available	53.5 % (3582/6691)	50.6 % (1338/2644)	54.8 % (1597/2912)	57.0 % (647/1135)	0.00025
Fasting LDL-cholesterol [mmol/L]	3.06 ± 0.97, n=3582	3.06 ± 0.99, n=1338	3.04 ± 0.95, n=1597	3.10 ± 0.98, n=647	0.47252
Absolute change [FU - BL]	-0.16 ± 0.83, n=3266	-0.11 ± 0.85, n=1209	-0.17 ± 0.81, n=1462	-0.21 ± 0.85, n=595	0.00614
Relative change [(FU - BL)/BL]	0.10 ± 2.24, n=3266	0.06 ± 1.64, n=1209	0.13 ± 2.65, n=1462	0.11 ± 2.22, n=595	0.00987
Fasting triglycerides available	58.8 % (3934/6691)	56.1 % (1484/2644)	61.8 % (1799/2912)	57.4 % (651/1135)	0.00006
Fasting triglycerides [mmol/L]	2.11 ± 1.36, n=3934	2.08 ± 1.28, n=1484	2.12 ± 1.45, n=1799	2.14 ± 1.27, n=651	0.53328
Absolute change [FU - BL]	-0.20 ± 1.30, n=3616	-0.15 ± 1.29, n=1348	-0.17 ± 1.28, n=1675	-0.40 ± 1.37, n=593	<.00001
Relative change [(FU - BL)/BL]	0.04 ± 1.38, n=3616	0.05 ± 0.65, n=1348	0.03 ± 1.14, n=1675	0.03 ± 2.63, n=593	<.00001
Fasting glucose available	70.6 % (4725/6691)	68.7 % (1817/2644)	73.5 % (2140/2912)	67.7 % (768/1135)	0.00003
Fasting glucose [mmol/L]	7.38 ± 2.16, n=4725	7.07 ± 2.00, n=1817	7.41 ± 2.06, n=2140	8.03 ± 2.60, n=768	<.00001
Absolute change [FU - BL]	-1.12 ± 2.84, n=4481	-0.70 ± 2.58, n=1735	-1.30 ± 2.78, n=2035	-1.64 ± 3.42, n=711	<.00001
Relative change [(FU - BL)/BL]	-0.07 ± 0.63, n=4481	-0.03 ± 0.64, n=1735	-0.10 ± 0.48, n=2035	-0.09 ± 0.91, n=711	<.00001
Postprandial glucose available	39.9 % (2672/6691)	34.9 % (924/2644)	44.5 % (1297/2912)	39.7 % (451/1135)	<.00001

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
Postprandial glucose [mmol/L]	8.76 ± 4.33, n=2672	8.46 ± 2.51, n=924	8.67 ± 2.84, n=1297	9.63 ± 8.62, n=451	<.00001
Absolute change [FU - BL]	-2.17 ± 4.99, n=2214	-1.54 ± 3.19, n=759	-2.54 ± 3.31, n=1083	-2.36 ± 9.72, n=372	<.00001
Relative change [(FU - BL)/BL]	-0.11 ± 1.06, n=2214	-0.07 ± 1.05, n=759	-0.13 ± 1.11, n=1083	-0.15 ± 0.96, n=372	<.00001
HbA1c [%]	7.05 ± 1.00, n=6075	6.79 ± 0.94, n=2363	7.09 ± 0.90, n=2691	7.56 ± 1.16, n=1021	<.00001
[HbA1c FU12 - target HbA1c]	0.16 ± 0.97, n=6075	0.29 ± 0.94, n=2363	0.09 ± 0.90, n=2691	0.06 ± 1.16, n=1021	<.00001
Target HbA1c met	53.1 % (3226/6075)	46.2 % (1092/2363)	56.8 % (1528/2691)	59.4 % (606/1021)	<.00001
Absolute change [FU - BL]	-0.73 ± 1.29, n=5892	-0.50 ± 1.19, n=2283	-0.81 ± 1.24, n=2619	-1.07 ± 1.49, n=990	<.00001
Relative change [(FU - BL)/BL]	-0.08 ± 0.13, n=5892	-0.05 ± 0.13, n=2283	-0.09 ± 0.13, n=2619	-0.11 ± 0.14, n=990	<.00001
Haemoglobin available	47.4 % (3174/6691)	41.4 % (1094/2644)	53.1 % (1546/2912)	47.0 % (534/1135)	<.00001
Haemoglobin [mmol/L]	8.35 ± 1.34, n=3174	8.35 ± 1.33, n=1094	8.36 ± 1.33, n=1546	8.33 ± 1.37, n=534	0.94618
Absolute change [FU - BL]	0.00 ± 0.77, n=2755	0.03 ± 0.79, n=924	-0.01 ± 0.81, n=1347	-0.01 ± 0.64, n=484	0.69706
Relative change [(FU - BL)/BL]	0.01 ± 0.15, n=2755	0.01 ± 0.13, n=924	0.01 ± 0.18, n=1347	0.00 ± 0.08, n=484	0.69494
Serum creatinine available	72.1 % (4824/6691)	71.7 % (1896/2644)	73.3 % (2134/2912)	70.0 % (794/1135)	0.08983
Serum creatinine [µmol/l]	84.71 ± 49.05, n=4824	84.71 ± 60.14, n=1896	84.66 ± 42.68, n=2134	84.85 ± 33.04, n=794	0.26547
Absolute change [FU - BL]	-0.05 ± 57.87, n=4438	-1.34 ± 81.43, n=1730	0.45 ± 40.40, n=1968	1.62 ± 15.57, n=740	0.14984
Relative change [(FU - BL)/BL]	0.03 ± 0.49, n=4438	0.04 ± 0.66, n=1730	0.02 ± 0.38, n=1968	0.04 ± 0.20, n=740	0.09886
Microalbustix albumin [mg/l]	19.83 ± 33.77, n=1481	21.04 ± 33.48, n=455	20.27 ± 33.76, n=790	16.04 ± 34.24, n=236	<.00001
Microalbustix creatinine [mg/dl]	43.58 ± 78.63, n=831	54.60 ± 81.73, n=249	45.23 ± 82.56, n=418	22.67 ± 56.99, n=164	<.00001
Macroalbuminuria: positive test	7.0 % (246/3531)	6.4 % (81/1256)	7.6 % (125/1646)	6.4 % (40/629)	0.39118
Macroalbuminuria: negative test	93.0 % (3285/3531)	93.6 % (1175/1256)	92.4 % (1521/1646)	93.6 % (589/629)	0.39118
Increased liver function readings	10.3 % (402/3900)	10.1 % (149/1477)	10.2 % (181/1769)	11.0 % (72/654)	0.80404

Patient characteristics at 24-month follow-up

Table 9-45 shows vital status and cause of death in the HbA1c treatment groups at 24-month follow-up.

Table 9-46 shows newly diagnosed diseases and other events in the HbA1c treatment groups at 24-month follow-up.

Table 9-47 shows absolute and relative changes in clinical parameters (i.e. SBP; DBP, Heart rate; Weight; BMI; Waist circumference) in the HbA1c treatment groups at 24-month follow-up.

Table 9-48 shows absolute and relative changes in laboratory values (i.e. Cholesterol; Glucose; Haemoglobin; Creatinine; Liver function) in the HbA1c treatment groups at 24-month follow-up.

Table 9-45. *Vital status and cause of death in the HbA1c treatment groups at 24-month follow-up.*

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
No. of patients with FU data	4130 (100.0 %)	1671 (40.5 %)	1808 (43.8 %)	651 (15.8 %)	
FU date missing	0.1 % (6/4130)	0.2 % (4/1671)	0.1 % (2/1808)	0.0 % (0/651)	0.34701
Vital status missing	0.1 % (4/4130)	0.1 % (2/1671)	0.1 % (2/1808)	0.0 % (0/651)	0.68503
No. of days until 24-month FU	726.0 (696.0, 736.0)	725.0 (699.0, 738.0)	723.0 (686.0, 735.0)	730.0 (712.0, 738.0)	<.00001
Cumulative 2-year Mortality	0.4 % (35/8567)	0.5 % (18/3342)	0.3 % (10/3625)	0.4 % (7/1600)	0.22417
Sudden cardiac death	14.3 % (5/35)	16.7 % (3/18)	0.0 % (0/10)	28.6 % (2/7)	0.23262
Other cardiovascular causes	14.3 % (5/35)	5.6 % (1/18)	20.0 % (2/10)	28.6 % (2/7)	0.27891
Cancer	34.3 % (12/35)	44.4 % (8/18)	20.0 % (2/10)	28.6 % (2/7)	0.40017
Other	25.7 % (9/35)	22.2 % (4/18)	40.0 % (4/10)	14.3 % (1/7)	0.43563
Unknown	11.4 % (4/35)	11.1 % (2/18)	20.0 % (2/10)	0.0 % (0/7)	0.44246
No. of days until death	259.5 (153.0, 471.0)	334.0 (170.0, 471.0)	259.5 (137.0, 290.0)	225.0 (151.0, 534.0)	0.60393

Table 9-46. *Newly diagnosed diseases and other events in the HbA1c treatment groups at 24-month follow-up.*

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
No. of patients with FU data	4130 (100.0 %)	1671 (40.5 %)	1808 (43.8 %)	651 (15.8 %)	
Coronary Heart Disease	0.3 % (11/4116)	0.2 % (3/1663)	0.2 % (4/1802)	0.6 % (4/651)	0.16920
Myocardial infarction	0.2 % (8/4115)	0.1 % (2/1662)	0.2 % (4/1802)	0.3 % (2/651)	0.61646
PCI	0.3 % (14/4115)	0.2 % (4/1662)	0.2 % (4/1802)	0.9 % (6/651)	0.02107
CABG	0.0 % (1/4115)	0.0 % (0/1662)	0.0 % (0/1802)	0.2 % (1/651)	0.06987
Peripheral angioplasty	0.0 % (2/4115)	0.1 % (1/1662)	0.0 % (0/1802)	0.2 % (1/651)	0.30125
Peripheral bypass surgery	0.0 % (1/4115)	0.0 % (0/1662)	0.0 % (0/1802)	0.2 % (1/651)	0.06987
Stroke/TIA	0.3 % (11/4115)	0.3 % (5/1662)	0.3 % (6/1802)	0.0 % (0/651)	0.34884
Heart Failure	0.2 % (10/4115)	0.2 % (4/1662)	0.3 % (5/1802)	0.2 % (1/651)	0.85930
NYHA I	10.0 % (1/10)	25.0 % (1/4)	0.0 % (0/5)	0.0 % (0/1)	0.43460
NYHA II	50.0 % (5/10)	50.0 % (2/4)	60.0 % (3/5)	0.0 % (0/1)	0.54881
NYHA III	40.0 % (4/10)	25.0 % (1/4)	40.0 % (2/5)	100.0 % (1/1)	0.39161
NYHA IV	0.0 % (0/10)	0.0 % (0/4)	0.0 % (0/5)	0.0 % (0/1)	
Peripheral arterial occlusive disease	0.1 % (4/4115)	0.1 % (2/1662)	0.1 % (2/1802)	0.0 % (0/651)	0.68378
Dyslipidemia	0.1 % (5/4115)	0.1 % (2/1662)	0.1 % (2/1802)	0.2 % (1/651)	0.96469
Autonomous neuropathy	0.2 % (8/4114)	0.1 % (1/1661)	0.2 % (3/1802)	0.6 % (4/651)	0.02315
Non-proliferative diabetic retinopathy	0.0 % (1/4114)	0.0 % (0/1661)	0.0 % (0/1802)	0.2 % (1/651)	0.06992
Proliferative diabetic retinopathy / laser coagulation	0.0 % (0/4114)	0.0 % (0/1661)	0.0 % (0/1802)	0.0 % (0/651)	
Diabetic macular edema	0.0 % (0/4114)	0.0 % (0/1661)	0.0 % (0/1802)	0.0 % (0/651)	
Blindness	0.0 % (0/4114)	0.0 % (0/1661)	0.0 % (0/1802)	0.0 % (0/651)	
Dialysis	0.0 % (2/4114)	0.1 % (1/1661)	0.1 % (1/1802)	0.0 % (0/651)	0.82692
Amputation	0.0 % (0/4130)	0.0 % (0/1671)	0.0 % (0/1808)	0.0 % (0/651)	
Foot					
Toes					

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
Upper extremities					
Lower extremities					
Rehospitalisation	3.2 % (131/4114)	3.3 % (55/1662)	2.8 % (51/1801)	3.8 % (25/651)	0.42341
Reasons					
Cardiac	30.5 % (40/131)	29.1 % (16/55)	27.5 % (14/51)	40.0 % (10/25)	0.51205
Diabetes	4.6 % (6/131)	5.5 % (3/55)	3.9 % (2/51)	4.0 % (1/25)	0.92031
Other	64.9 % (85/131)	61.8 % (34/55)	70.6 % (36/51)	60.0 % (15/25)	0.54418
Unknown	2.3 % (3/131)	5.5 % (3/55)	0.0 % (0/51)	0.0 % (0/25)	0.11987
Duration [weeks]	1.0 (1.0, 2.0)	2.0 (1.0, 2.0)	1.0 (1.0, 2.0)	1.0 (1.0, 2.0)	0.25350
Rehabilitation measures	1.2 % (50/4116)	1.2 % (20/1662)	1.1 % (20/1803)	1.5 % (10/651)	0.69448
Reasons					
Cardiac	24.0 % (12/50)	30.0 % (6/20)	10.0 % (2/20)	40.0 % (4/10)	0.13894
Diabetes	4.0 % (2/50)	5.0 % (1/20)	5.0 % (1/20)	0.0 % (0/10)	0.77073
Other	70.0 % (35/50)	65.0 % (13/20)	85.0 % (17/20)	50.0 % (5/10)	0.11732
Unknown	4.0 % (2/50)	5.0 % (1/20)	0.0 % (0/20)	10.0 % (1/10)	0.40194
As out-patient	12.0 % (6/50)	5.0 % (1/20)	20.0 % (4/20)	10.0 % (1/10)	0.33655
As in-patient	88.0 % (44/50)	95.0 % (19/20)	80.0 % (16/20)	90.0 % (9/10)	0.33655
Duration [weeks]	3.0 (3.0, 4.0)	3.0 (3.0, 4.0)	3.0 (3.0, 4.0)	3.0 (3.0, 4.0)	0.68640
General practitioner consultations	92.8 % (3819/4116)	92.7 % (1541/1662)	93.4 % (1684/1803)	91.2 % (594/651)	0.18852
No. of contacts	5.0 (3.0, 10.0)	6.0 (3.0, 10.0)	5.0 (4.0, 8.0)	6.0 (4.0, 10.0)	0.00231
Specialist physician consultations	62.4 % (2569/4116)	57.7 % (959/1662)	67.6 % (1218/1803)	60.2 % (392/651)	<.00001
No. of contacts	2.0 (1.0, 4.0)	2.0 (1.0, 4.0)	2.0 (1.0, 4.0)	2.0 (1.0, 4.0)	0.16326

Table 9-47. *Absolute and relative changes in clinical parameters in the HbA1c treatment groups at 24-month follow-up.*

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
No. of patients with FU data	4130 (100.0 %)	1671 (40.5 %)	1808 (43.8 %)	651 (15.8 %)	
Systolic blood pressure	134.97 ± 12.91, n=4111	134.84 ± 12.67, n=1660	134.71 ± 13.05, n=1800	135.99 ± 13.06, n=651	0.02557
Absolute change (FU24-Basis)	-5.55 ± 16.91, n=4111	-4.79 ± 17.16, n=1660	-6.16 ± 16.62, n=1800	-5.79 ± 17.04, n=651	0.02868
Relative change (FU24-Basis/Basis)	-0.03 ± 0.12, n=4111	-0.03 ± 0.12, n=1660	-0.04 ± 0.12, n=1800	-0.03 ± 0.12, n=651	0.01936
[SBP FU24 - target SBP]	0.64 ± 13.11, n=4097	2.94 ± 12.84, n=1656	-0.67 ± 13.11, n=1798	-1.59 ± 12.91, n=643	<.00001
Target SBP met	59.5 % (2447/4111)	52.1 % (865/1660)	63.2 % (1137/1800)	68.4 % (445/651)	<.00001
Diastolic blood pressure	80.58 ± 7.96, n=4111	80.75 ± 8.10, n=1660	80.43 ± 7.94, n=1800	80.56 ± 7.67, n=651	0.39682
Absolute change [FU - BL]	-2.49 ± 10.39, n=4111	-2.15 ± 10.72, n=1660	-2.64 ± 10.10, n=1800	-2.96 ± 10.30, n=651	0.09942
Relative change [(FU - BL)/BL]	-0.02 ± 0.13, n=4111	-0.02 ± 0.14, n=1660	-0.02 ± 0.13, n=1800	-0.03 ± 0.14, n=651	0.09126
[SBP FU24 - target SBP]	0.64 ± 13.11, n=4097	2.94 ± 12.84, n=1656	-0.67 ± 13.11, n=1798	-1.59 ± 12.91, n=643	<.00001
Target DBP met	76.2 % (3133/4111)	68.4 % (1136/1660)	80.8 % (1454/1800)	83.4 % (543/651)	<.00001
Heart rate [/min]	74.00 ± 8.62, n=4108	74.01 ± 9.00, n=1657	73.84 ± 8.29, n=1800	74.43 ± 8.49, n=651	0.39261
Absolute change [FU - BL]	-1.02 ± 10.68, n=4099	-0.39 ± 10.92, n=1650	-1.38 ± 10.21, n=1798	-1.63 ± 11.25, n=651	0.00164
Relative change [(FU - BL)/BL]	-0.00 ± 0.14, n=4099	0.01 ± 0.15, n=1650	-0.01 ± 0.14, n=1798	-0.01 ± 0.14, n=651	0.00217
Weight [kg]	88.87 ± 18.17, n=4110	88.58 ± 18.53, n=1660	88.57 ± 17.78, n=1800	90.47 ± 18.26, n=650	0.04411
Absolute change [FU - BL]	-1.27 ± 6.02, n=4110	-1.07 ± 5.85, n=1660	-1.44 ± 6.23, n=1800	-1.28 ± 5.88, n=650	0.11157
Relative change [(FU - BL)/BL]	-0.01 ± 0.07, n=4110	-0.01 ± 0.06, n=1660	-0.01 ± 0.07, n=1800	-0.01 ± 0.07, n=650	0.12023
BMI [kg/m2]	30.74 ± 5.76, n=4110	30.69 ± 5.96, n=1660	30.65 ± 5.62, n=1800	31.12 ± 5.59, n=650	0.07174
Absolute change [FU - BL]	-0.43 ± 2.08, n=4110	-0.36 ± 2.02, n=1660	-0.49 ± 2.14, n=1800	-0.44 ± 2.08, n=650	0.08527
Relative change [(FU - BL)/BL]	-0.01 ± 0.07, n=4110	-0.01 ± 0.06, n=1660	-0.01 ± 0.07, n=1800	-0.01 ± 0.07, n=650	0.12059
BMI < 25	12.5 % (512/4110)	13.7 % (228/1660)	11.7 % (211/1800)	11.2 % (73/650)	0.11805
BMI: 25 - 30	39.3 % (1614/4110)	38.7 % (643/1660)	41.1 % (739/1800)	35.7 % (232/650)	0.04750

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
BMI > 30	48.3 % (1984/4110)	47.5 % (789/1660)	47.2 % (850/1800)	53.1 % (345/650)	0.02773
Waist circumference [cm]	106.94 ± 16.17, n=1200	106.84 ± 15.23, n=443	106.08 ± 15.93, n=626	111.39 ± 19.54, n=131	0.00466
Absolute change [FU - BL]	-0.96 ± 9.45, n=1048	-1.06 ± 9.06, n=388	-1.17 ± 9.28, n=554	0.45 ± 11.46, n=106	0.24444
Relative change [(FU - BL)/BL]	-0.01 ± 0.09, n=1048	-0.01 ± 0.08, n=388	-0.01 ± 0.08, n=554	0.01 ± 0.11, n=106	0.16567
Diabetes training FU12+FU24	45.6 % (1881/4129)	50.0 % (836/1671)	40.8 % (737/1807)	47.3 % (308/651)	<.00001
Participation in DMP diabetes	81.6 % (3354/4111)	81.2 % (1347/1659)	83.1 % (1496/1801)	78.5 % (511/651)	0.03122

Table 9-48. *Absolute and relative changes in laboratory values in the HbA1c treatment groups at 24-month follow-up.*

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
No. of patients with FU data	4130 (100.0 %)	1671 (40.5 %)	1808 (43.8 %)	651 (15.8 %)	
Total fasting cholesterol available	67.8 % (2799/4130)	64.4 % (1076/1671)	70.1 % (1267/1808)	70.0 % (456/651)	0.00065
Total fasting cholesterol [mmol/L]	9.74 ± 3.05, n=2799	9.77 ± 3.19, n=1076	9.75 ± 2.87, n=1267	9.60 ± 3.21, n=456	0.44295
Absolute change [FU - BL]	4.42 ± 2.77, n=2652	4.45 ± 2.91, n=1019	4.47 ± 2.56, n=1200	4.24 ± 2.96, n=433	0.32044
Relative change [(FU - BL)/BL]	0.87 ± 0.54, n=2652	0.87 ± 0.56, n=1019	0.89 ± 0.52, n=1200	0.82 ± 0.56, n=433	0.18046
Fasting HDL-cholesterol available	52.2 % (2156/4130)	48.6 % (812/1671)	54.7 % (989/1808)	54.5 % (355/651)	0.00065
Fasting HDL-cholesterol [mmol/L]	1.27 ± 0.36, n=2156	1.30 ± 0.33, n=812	1.26 ± 0.37, n=989	1.26 ± 0.39, n=355	0.01077
Absolute change [FU - BL]	0.02 ± 0.32, n=1987	0.01 ± 0.28, n=744	0.03 ± 0.29, n=913	0.02 ± 0.45, n=330	0.18910
Relative change [(FU - BL)/BL]	0.05 ± 0.29, n=1987	0.04 ± 0.23, n=744	0.06 ± 0.36, n=913	0.05 ± 0.23, n=330	0.17636
Fasting LDL-cholesterol available	50.7 % (2095/4130)	46.1 % (770/1671)	53.2 % (962/1808)	55.8 % (363/651)	<.00001
Fasting LDL-cholesterol [mmol/L]	3.02 ± 0.93, n=2095	3.06 ± 0.98, n=770	2.98 ± 0.89, n=962	3.02 ± 0.88, n=363	0.58245
Absolute change [FU - BL]	-0.17 ± 0.82, n=1917	-0.11 ± 0.81, n=696	-0.20 ± 0.82, n=884	-0.22 ± 0.85, n=337	0.05924
Relative change [(FU - BL)/BL]	0.08 ± 1.90, n=1917	0.11 ± 2.20, n=696	0.09 ± 1.98, n=884	-0.02 ± 0.47, n=337	0.12685
Fasting triglycerides available	59.0 % (2437/4130)	55.7 % (930/1671)	62.6 % (1131/1808)	57.8 % (376/651)	0.00015
Fasting triglycerides [mmol/L]	2.02 ± 1.19, n=2437	2.02 ± 1.21, n=930	1.98 ± 1.11, n=1131	2.13 ± 1.38, n=376	0.02775
Absolute change [FU - BL]	-0.25 ± 1.35, n=2259	-0.16 ± 1.30, n=851	-0.27 ± 1.27, n=1057	-0.42 ± 1.65, n=351	0.00056
Relative change [(FU - BL)/BL]	-0.00 ± 0.50, n=2259	0.05 ± 0.56, n=851	-0.02 ± 0.48, n=1057	-0.07 ± 0.39, n=351	0.00111
Fasting glucose available	72.0 % (2974/4130)	69.4 % (1160/1671)	74.9 % (1354/1808)	70.7 % (460/651)	0.00112
Fasting glucose [mmol/L]	7.31 ± 2.10, n=2974	7.02 ± 1.94, n=1160	7.31 ± 2.06, n=1354	8.02 ± 2.41, n=460	<.00001
Absolute change [FU - BL]	-1.12 ± 2.84, n=2815	-0.67 ± 2.63, n=1084	-1.32 ± 2.75, n=1294	-1.68 ± 3.36, n=437	<.00001
Relative change [(FU - BL)/BL]	-0.07 ± 0.50, n=2815	-0.03 ± 0.31, n=1084	-0.09 ± 0.64, n=1294	-0.12 ± 0.37, n=437	<.00001
Postprandial glucose available	40.1 % (1656/4130)	35.1 % (586/1671)	44.8 % (810/1808)	39.9 % (260/651)	<.00001

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
Postprandial glucose [mmol/L]	8.64 ± 2.71, n=1656	8.53 ± 2.78, n=586	8.44 ± 2.65, n=810	9.49 ± 2.60, n=260	<.00001
Absolute change [FU - BL]	-2.27 ± 3.42, n=1373	-1.32 ± 3.36, n=480	-2.62 ± 3.12, n=673	-3.26 ± 3.91, n=220	<.00001
Relative change [(FU - BL)/BL]	-0.09 ± 1.20, n=1373	0.00 ± 1.34, n=480	-0.13 ± 1.19, n=673	-0.17 ± 0.82, n=220	<.00001
HbA1c [%]	7.01 ± 0.99, n=3783	6.80 ± 0.97, n=1499	7.04 ± 0.91, n=1679	7.42 ± 1.08, n=605	<.00001
[HbA1c FU24 - target HbA1c]	0.12 ± 0.98, n=3783	0.30 ± 0.97, n=1499	0.04 ± 0.91, n=1679	-0.08 ± 1.08, n=605	<.00001
Target HbA1c met	55.8 % (2112/3783)	46.0 % (690/1499)	61.5 % (1032/1679)	64.5 % (390/605)	<.00001
Absolute change [FU - BL]	-0.76 ± 1.34, n=3662	-0.48 ± 1.28, n=1450	-0.83 ± 1.26, n=1629	-1.25 ± 1.53, n=583	<.00001
Relative change [(FU - BL)/BL]	-0.08 ± 0.14, n=3662	-0.05 ± 0.15, n=1450	-0.09 ± 0.14, n=1629	-0.13 ± 0.15, n=583	<.00001
Haemoglobin available	46.6 % (1924/4130)	39.4 % (658/1671)	53.3 % (963/1808)	46.5 % (303/651)	<.00001
Haemoglobin [mmol/L]	8.54 ± 1.11, n=1924	8.48 ± 1.17, n=658	8.61 ± 1.00, n=963	8.47 ± 1.27, n=303	0.03972
Absolute change [FU - BL]	-0.01 ± 0.74, n=1663	0.00 ± 0.86, n=533	-0.01 ± 0.66, n=850	-0.03 ± 0.75, n=280	0.75241
Relative change [(FU - BL)/BL]	0.00 ± 0.11, n=1663	0.01 ± 0.14, n=533	0.00 ± 0.09, n=850	0.00 ± 0.10, n=280	0.69553
Serum creatinine available	71.9 % (2969/4130)	71.9 % (1201/1671)	72.9 % (1318/1808)	69.1 % (450/651)	0.18512
Serum creatinine [µmol/l]	87.31 ± 146.53, n=2969	86.41 ± 67.99, n=1201	89.47 ± 209.68, n=1318	83.37 ± 24.37, n=450	0.62731
Absolute change [FU - BL]	0.28 ± 33.33, n=2721	0.38 ± 45.36, n=1089	-0.38 ± 23.33, n=1217	1.97 ± 16.98, n=415	0.01352
Relative change [(FU - BL)/BL]	0.03 ± 0.26, n=2721	0.04 ± 0.34, n=1089	0.02 ± 0.19, n=1217	0.04 ± 0.20, n=415	0.01135
Microalbustix albumin [mg/l]	16.79 ± 31.45, n=900	16.14 ± 28.32, n=259	17.32 ± 32.68, n=512	15.98 ± 32.59, n=129	0.12606
Microalbustix creatinine [mg/dl]	38.16 ± 71.39, n=518	43.44 ± 69.50, n=158	45.10 ± 79.48, n=265	10.04 ± 35.16, n=95	<.00001
Macroalbuminuria: positive test	5.7 % (128/2257)	3.9 % (33/843)	6.6 % (69/1050)	7.1 % (26/364)	0.01900
Macroalbuminuria: negative test	94.3 % (2129/2257)	96.1 % (810/843)	93.4 % (981/1050)	92.9 % (338/364)	0.01900
Increased liver function readings	8.4 % (207/2452)	8.4 % (82/973)	8.2 % (88/1078)	9.2 % (37/401)	0.80724

9.4.1.3 Therapeutic patterns

Therapeutic patterns at 6 months follow-up

Table 9-49 shows anti-diabetic therapy in the in the HbA1c treatment groups at 6-month follow-up (i.e. Metformin; Sulfonylurea drugs; Glucosidase inhibitors; Glinide; Glitazone; DPP-4 inhibitors; GLP-1 analogs; SGTL-2 inhibitors; Total number of antidiabetics; Insulin; Novartis drugs).

Table 9-50 shows anti-hypertensive therapy in the in the HbA1c treatment groups at 6-month follow-up (i.e. ACE inhibitors; ARB; Direct renin inhibitor; Beta-blocker; Calcium channel blocker; Diuretic drugs; Total number of antihypertensive drugs; Fixed-dose combinations; Novartis drugs).

Table 9-51 shows hypoglycemic events in the in the HbA1c treatment groups at 6-month follow-up (i.e. Number of events; Type of events; Help needed).

Table 9-49. *Anti-diabetic therapy in the in the HbA1c treatment groups at 6-month follow-up.*

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
No. of patients with FU data	7355 (100.0 %)	2886 (39.2 %)	3197 (43.5 %)	1272 (17.3 %)	
Glucosidase inhibitors	1.1 % (83/7349)	1.0 % (28/2882)	1.4 % (46/3197)	0.7 % (9/1270)	0.06727
Glucosidase inhibitors, dosage [mg/day]	144.30 ± 82.24, n=83	102.39 ± 44.79, n=28	166.52 ± 90.31, n=46	161.11 ± 85.80, n=9	0.00723
Substance					
Acarbose	91.6 % (76/83)	85.7 % (24/28)	93.5 % (43/46)	100.0 % (9/9)	0.31848
Miglitol	7.2 % (6/83)	14.3 % (4/28)	4.3 % (2/46)	0.0 % (0/9)	0.18733
Other	1.2 % (1/83)	0.0 % (0/28)	2.2 % (1/46)	0.0 % (0/9)	0.66559
Glinide	3.7 % (275/7339)	2.5 % (73/2872)	3.8 % (123/3197)	6.2 % (79/1270)	<.00001
Glinide, dosage [mg/day]	13.98 ± 54.37, n=274	11.74 ± 45.69, n=72	14.38 ± 56.52, n=123	15.39 ± 58.66, n=79	0.60815
Substance					
Nateglinide	2.9 % (8/275)	2.7 % (2/73)	3.3 % (4/123)	2.5 % (2/79)	0.95195
Repaglinide	93.5 % (257/275)	95.9 % (70/73)	91.1 % (112/123)	94.9 % (75/79)	0.34168
Other	3.6 % (10/275)	1.4 % (1/73)	5.7 % (7/123)	2.5 % (2/79)	0.24326
Glitazone	0.5 % (36/7349)	0.5 % (13/2882)	0.7 % (21/3197)	0.2 % (2/1270)	0.09088
Glitazone, dosage [mg/day]	38.64 ± 22.49, n=36	31.54 ± 10.28, n=13	45.95 ± 25.18, n=21	8.00 ± 9.90, n=2	0.01192
Substance					
Pioglitazon	86.1 % (31/36)	100.0 % (13/13)	76.2 % (16/21)	100.0 % (2/2)	0.12572
Other	13.9 % (5/36)	0.0 % (0/13)	23.8 % (5/21)	0.0 % (0/2)	0.12572
DPP-4 inhibitors	62.2 % (4560/7337)	58.5 % (1679/2869)	65.7 % (2102/3197)	61.3 % (779/1271)	<.00001
DPP-4 inhibitors, dosage [mg/day]	84.85 ± 33.63, n=4560	83.86 ± 33.10, n=1679	85.30 ± 34.65, n=2102	85.76 ± 31.92, n=779	0.01263
Substance					
Sitagliptin	30.0 % (1367/4560)	29.8 % (501/1679)	29.6 % (623/2102)	31.2 % (243/779)	0.71196
Vildagliptin	65.2 % (2973/4560)	65.6 % (1102/1679)	65.5 % (1377/2102)	63.4 % (494/779)	0.51624
Linagliptin	0.0 % (1/4560)	0.1 % (1/1679)	0.0 % (0/2102)	0.0 % (0/779)	0.42395
Saxagliptin	4.5 % (204/4560)	4.1 % (68/1679)	4.6 % (97/2102)	5.0 % (39/779)	0.51679
Other	0.3 % (15/4560)	0.4 % (7/1679)	0.2 % (5/2102)	0.4 % (3/779)	0.60561
GLP-1 analogs/mimetics	5.4 % (394/7352)	4.7 % (135/2885)	5.8 % (184/3197)	5.9 % (75/1270)	0.11272
GLP-1 analogs/mimetics, dosage [mg/day]	6.95 ± 13.31, n=393	6.92 ± 12.31, n=135	7.18 ± 14.45, n=183	6.43 ± 12.26, n=75	0.34876
Substance					

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
Exenatide	39.4 % (155/393)	37.8 % (51/135)	38.8 % (71/183)	44.0 % (33/75)	0.65682
Liraglutide	53.2 % (209/393)	49.6 % (67/135)	57.4 % (105/183)	49.3 % (37/75)	0.29763
Other	7.4 % (29/393)	12.6 % (17/135)	3.8 % (7/183)	6.7 % (5/75)	0.01224
SGTL-2 inhibitors	2.1 % (154/7353)	2.0 % (57/2886)	2.0 % (65/3197)	2.5 % (32/1270)	0.50178
SGTL-2 inhibitors, dosage [mg/day]	13.14 ± 15.70, n=153	14.56 ± 18.03, n=57	11.66 ± 12.37, n=64	13.59 ± 17.38, n=32	0.11700
Substance					
Dapagliflozin	96.1 % (147/153)	94.7 % (54/57)	96.9 % (62/64)	96.9 % (31/32)	0.80495
Other	3.9 % (6/153)	5.3 % (3/57)	3.1 % (2/64)	3.1 % (1/32)	0.80495
Insulin(rapid-acting or long-acting or Pre-mixed)	17.1 % (1257/7355)	12.0 % (345/2886)	19.2 % (613/3197)	23.5 % (299/1272)	<.00001
Rapid-acting insulin	5.8 % (425/7353)	4.6 % (134/2886)	5.7 % (182/3197)	8.6 % (109/1270)	<.00001
Human insulin	45.9 % (195/425)	50.7 % (68/134)	42.3 % (77/182)	45.9 % (50/109)	0.33066
Analogues	54.1 % (230/425)	49.3 % (66/134)	57.7 % (105/182)	54.1 % (59/109)	0.33066
Syringe	3.1 % (13/425)	2.2 % (3/134)	2.7 % (5/182)	4.6 % (5/109)	0.54279
Pen	96.9 % (412/425)	97.8 % (131/134)	97.3 % (177/182)	95.4 % (104/109)	0.54279
Pump	0.0 % (0/425)	0.0 % (0/134)	0.0 % (0/182)	0.0 % (0/109)	
Other	0.0 % (0/425)	0.0 % (0/134)	0.0 % (0/182)	0.0 % (0/109)	
U-40	19.0 % (80/422)	24.8 % (33/133)	15.0 % (27/180)	18.3 % (20/109)	0.08944
U-100	81.0 % (342/422)	75.2 % (100/133)	85.0 % (153/180)	81.7 % (89/109)	0.08944
1x insulin/day	9.7 % (41/424)	12.8 % (17/133)	7.1 % (13/182)	10.1 % (11/109)	0.24323
2x insulin/day	14.9 % (63/424)	21.1 % (28/133)	9.9 % (18/182)	15.6 % (17/109)	0.02202
3x insulin/day	74.1 % (314/424)	66.2 % (88/133)	81.9 % (149/182)	70.6 % (77/109)	0.00463
4x insulin/day	1.4 % (6/424)	0.0 % (0/133)	1.1 % (2/182)	3.7 % (4/109)	0.04951
Long-acting insulin	15.8 % (1159/7353)	10.8 % (312/2886)	17.9 % (573/3197)	21.6 % (274/1270)	<.00001
Human insulin	30.0 % (348/1159)	33.3 % (104/312)	26.2 % (150/573)	34.3 % (94/274)	0.01784
Analogues	70.0 % (811/1159)	66.7 % (208/312)	73.8 % (423/573)	65.7 % (180/274)	0.01784

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
Syringe	5.3 % (61/1159)	3.8 % (12/312)	5.6 % (32/573)	6.2 % (17/274)	0.39416
Pen	94.5 % (1095/1159)	96.2 % (300/312)	93.9 % (538/573)	93.8 % (257/274)	0.31639
Pump	0.2 % (2/1159)	0.0 % (0/312)	0.3 % (2/573)	0.0 % (0/274)	0.35899
Other	0.1 % (1/1159)	0.0 % (0/312)	0.2 % (1/573)	0.0 % (0/274)	0.59942
U-40	15.3 % (176/1154)	17.3 % (54/312)	11.8 % (67/569)	20.1 % (55/273)	0.00334
U-100	84.7 % (978/1154)	82.7 % (258/312)	88.2 % (502/569)	79.9 % (218/273)	0.00334
1x insulin/day	86.0 % (997/1159)	84.3 % (263/312)	86.9 % (498/573)	86.1 % (236/274)	0.56175
2x insulin/day	12.4 % (144/1159)	12.2 % (38/312)	12.4 % (71/573)	12.8 % (35/274)	0.97603
3x insulin/day	1.5 % (17/1159)	3.2 % (10/312)	0.7 % (4/573)	1.1 % (3/274)	0.01042
4x insulin/day	0.1 % (1/1159)	0.3 % (1/312)	0.0 % (0/573)	0.0 % (0/274)	0.25703
Pre-mixed insulin	2.0 % (148/7353)	1.0 % (28/2886)	2.3 % (74/3197)	3.6 % (46/1270)	<.00001
Human insulin	61.5 % (91/148)	60.7 % (17/28)	64.9 % (48/74)	56.5 % (26/46)	0.65622
Analogues	38.5 % (57/148)	39.3 % (11/28)	35.1 % (26/74)	43.5 % (20/46)	0.65622
Syringe	4.1 % (6/148)	0.0 % (0/28)	2.7 % (2/74)	8.7 % (4/46)	0.13013
Pen	95.9 % (142/148)	100.0 % (28/28)	97.3 % (72/74)	91.3 % (42/46)	0.13013
Pump	0.0 % (0/148)	0.0 % (0/28)	0.0 % (0/74)	0.0 % (0/46)	
Other	0.0 % (0/148)	0.0 % (0/28)	0.0 % (0/74)	0.0 % (0/46)	
U-40	16.2 % (24/148)	21.4 % (6/28)	13.5 % (10/74)	17.4 % (8/46)	0.60517
U-100	83.8 % (124/148)	78.6 % (22/28)	86.5 % (64/74)	82.6 % (38/46)	0.60517
1x insulin/day	11.5 % (17/148)	7.1 % (2/28)	5.4 % (4/74)	23.9 % (11/46)	0.00610
2x insulin/day	85.1 % (126/148)	89.3 % (25/28)	91.9 % (68/74)	71.7 % (33/46)	0.00834
3x insulin/day	2.7 % (4/148)	3.6 % (1/28)	1.4 % (1/74)	4.3 % (2/46)	0.58635
4x insulin/day	0.7 % (1/148)	0.0 % (0/28)	1.4 % (1/74)	0.0 % (0/46)	0.60447
Fixed-dose combination metformin / DPP-4 inhibitor	76.2 % (2808/3685)	76.3 % (1001/1312)	75.1 % (1286/1713)	78.9 % (521/660)	0.13963
Novartis drugs					
Vildagliptin / Metformin					

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
Eucreas	91.3 % (1791/1962)	92.2 % (638/692)	90.5 % (831/918)	91.5 % (322/352)	0.49429
Icandra	8.7 % (171/1962)	7.8 % (54/692)	9.5 % (87/918)	8.5 % (30/352)	0.49429
Vildagliptin					
Galvus	85.7 % (866/1010)	82.4 % (338/410)	89.1 % (408/458)	84.5 % (120/142)	0.01815
Jalra	14.3 % (144/1010)	17.6 % (72/410)	10.9 % (50/458)	15.5 % (22/142)	0.01815
Nateglinide					
STARLIX	100.0 % (8/8)	100.0 % (2/2)	100.0 % (4/4)	100.0 % (2/2)	
Other	0.0 % (0/8)	0.0 % (0/2)	0.0 % (0/4)	0.0 % (0/2)	

Table 9-50. *Anti-hypertensive therapy in the HbA1c treatment groups at 6-month follow-up.*

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
No. of patients with FU data	7355 (100.0 %)	2886 (39.2 %)	3197 (43.5 %)	1272 (17.3 %)	
ACE inhibitors	52.4 % (3852/7347)	51.4 % (1482/2884)	53.8 % (1718/3195)	51.4 % (652/1268)	0.12987
ACE inhibitors, dosage [mg/day]	10.56 ± 12.51, n=3841	10.51 ± 12.44, n=1471	10.39 ± 12.17, n=1718	11.14 ± 13.51, n=652	0.00738
Substance					
Captopril	2.6 % (100/3847)	3.0 % (44/1477)	2.4 % (41/1718)	2.3 % (15/652)	0.50205
Enalapril	17.7 % (680/3847)	18.8 % (277/1477)	16.6 % (285/1718)	18.1 % (118/652)	0.26518
Lisinopril	11.6 % (448/3847)	11.6 % (171/1477)	11.8 % (203/1718)	11.3 % (74/652)	0.94617
Ramipril	65.1 % (2504/3847)	64.1 % (947/1477)	66.2 % (1137/1718)	64.4 % (420/652)	0.43892
Trandolapril	0.2 % (7/3847)	0.1 % (2/1477)	0.2 % (3/1718)	0.3 % (2/652)	0.69063
Other	2.8 % (108/3847)	2.4 % (36/1477)	2.9 % (49/1718)	3.5 % (23/652)	0.36913
Angiotensin receptor blocker (ARB)	28.3 % (2080/7342)	28.3 % (815/2879)	29.0 % (926/3195)	26.7 % (339/1268)	0.32305
ARB, dosage [mg/day]	116.30 ± 115.86, n=2077	119.01 ± 120.08, n=812	112.43 ± 111.21, n=926	120.37 ± 117.99, n=339	0.59844
Substance					
Candesartan	22.5 % (468/2080)	21.7 % (177/815)	22.1 % (205/926)	25.4 % (86/339)	0.37618
Irbesartan	5.6 % (116/2080)	6.1 % (50/815)	5.3 % (49/926)	5.0 % (17/339)	0.66080
Losartan	7.5 % (156/2080)	7.2 % (59/815)	7.5 % (69/926)	8.3 % (28/339)	0.83320
Valsartan	40.0 % (833/2080)	39.9 % (325/815)	40.7 % (377/926)	38.6 % (131/339)	0.79493
Other	24.4 % (507/2080)	25.0 % (204/815)	24.4 % (226/926)	22.7 % (77/339)	0.70539
Direct renin inhibitor	0.4 % (30/7341)	0.5 % (15/2878)	0.3 % (11/3195)	0.3 % (4/1268)	0.47439
Direct renin inhibitor, dosage [mg/day]	200.57 ± 89.72, n=30	181.07 ± 81.71, n=15	245.45 ± 75.68, n=11	150.25 ± 122.07, n=4	0.10135
Beta-blocker	47.9 % (3517/7345)	47.2 % (1361/2882)	48.2 % (1540/3195)	48.6 % (616/1268)	0.64488
Beta-blocker, dosage [mg/day]	54.09 ± 62.19, n=3510	52.07 ± 61.16, n=1354	57.74 ± 63.59, n=1540	49.41 ± 60.49, n=616	0.00057
Substance					
Metoprolol	45.6 % (1602/3516)	44.7 % (608/1360)	47.9 % (737/1540)	41.7 % (257/616)	0.02551
Bisoprolol	40.8 % (1436/3516)	42.4 % (576/1360)	38.1 % (587/1540)	44.3 % (273/616)	0.01057
Nebivolol	5.3 % (188/3516)	5.7 % (77/1360)	4.8 % (74/1540)	6.0 % (37/616)	0.42981
Carvedilol	4.8 % (169/3516)	4.0 % (54/1360)	5.6 % (87/1540)	4.5 % (28/616)	0.10230

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
Other	3.4 % (121/3516)	3.3 % (45/1360)	3.6 % (55/1540)	3.4 % (21/616)	0.92671
Calcium channel blocker	28.5 % (2093/7341)	26.8 % (770/2878)	29.1 % (931/3195)	30.9 % (392/1268)	0.01378
Calcium channel blocker, dosage [mg/day]	17.94 ± 42.51, n=2090	15.73 ± 36.45, n=767	19.44 ± 46.31, n=931	18.71 ± 44.01, n=392	0.45495
Substance					
Amlodipine	74.8 % (1565/2093)	73.8 % (568/770)	75.9 % (707/931)	74.0 % (290/392)	0.54428
Nifedipine	2.6 % (54/2093)	2.7 % (21/770)	2.1 % (20/931)	3.3 % (13/392)	0.44875
Nisoldipine	0.0 % (1/2093)	0.0 % (0/770)	0.1 % (1/931)	0.0 % (0/392)	0.53560
Nimodipine	0.0 % (1/2093)	0.1 % (1/770)	0.0 % (0/931)	0.0 % (0/392)	0.42337
Diltiazem	0.5 % (11/2093)	0.5 % (4/770)	0.3 % (3/931)	1.0 % (4/392)	0.27626
Verapamil	3.2 % (68/2093)	2.5 % (19/770)	3.5 % (33/931)	4.1 % (16/392)	0.26992
Gallopamil	0.0 % (0/2093)	0.0 % (0/770)	0.0 % (0/931)	0.0 % (0/392)	
Felodipine	3.0 % (63/2093)	2.5 % (19/770)	3.7 % (34/931)	2.6 % (10/392)	0.30524
Nitrendipine	4.3 % (90/2093)	4.5 % (35/770)	4.7 % (44/931)	2.8 % (11/392)	0.26589
Lercanidipine	10.3 % (216/2093)	12.3 % (95/770)	8.3 % (77/931)	11.2 % (44/392)	0.01870
Nilvadipine	0.0 % (1/2093)	0.0 % (0/770)	0.1 % (1/931)	0.0 % (0/392)	0.53560
Manidipine	0.0 % (1/2093)	0.1 % (1/770)	0.0 % (0/931)	0.0 % (0/392)	0.42337
Isradipine	0.1 % (2/2093)	0.3 % (2/770)	0.0 % (0/931)	0.0 % (0/392)	0.17910
Other	1.0 % (20/2093)	0.6 % (5/770)	1.2 % (11/931)	1.0 % (4/392)	0.52662
Diuretic drugs	43.7 % (3207/7344)	41.4 % (1193/2881)	44.3 % (1414/3195)	47.3 % (600/1268)	0.00130
Diuretic drugs, dosage [mg/day]	23.16 ± 23.66, n=3201	23.15 ± 26.20, n=1187	22.67 ± 19.71, n=1414	24.33 ± 26.68, n=600	0.88836
Substance					
Furosemide	8.6 % (276/3207)	7.0 % (83/1193)	9.5 % (134/1414)	9.8 % (59/600)	0.03624
Torasemide	23.4 % (752/3207)	22.4 % (267/1193)	23.2 % (328/1414)	26.2 % (157/600)	0.19421
Bumetanide	0.0 % (1/3207)	0.0 % (0/1193)	0.1 % (1/1414)	0.0 % (0/600)	0.53035
Etacrynic acid	0.0 % (1/3207)	0.0 % (0/1193)	0.1 % (1/1414)	0.0 % (0/600)	0.53035
Piretanide	1.1 % (35/3207)	1.3 % (15/1193)	1.1 % (15/1414)	0.8 % (5/600)	0.70938
Hydrochlorothiazide	68.8 % (2205/3207)	71.7 % (855/1193)	67.8 % (959/1414)	65.2 % (391/600)	0.01178
Clopamid	0.2 % (8/3207)	0.2 % (2/1193)	0.2 % (3/1414)	0.5 % (3/600)	0.38413
Other	8.6 % (276/3207)	7.5 % (89/1193)	9.2 % (130/1414)	9.5 % (57/600)	0.19968
Other anti-hypertensive therapy	10.6 % (776/7331)	9.3 % (268/2868)	11.0 % (350/3195)	12.5 % (158/1268)	0.00731
Fixed-dose combinations					

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
Fixed-dose combination ARB/calcium channel blocker/diuretic	71.7 % (436/608)	70.7 % (157/222)	72.0 % (198/275)	73.0 % (81/111)	0.90223
Fixed-dose combination ACE inhibitor/diuretic	49.3 % (804/1630)	51.5 % (313/608)	49.4 % (354/717)	44.9 % (137/305)	0.17374
Fixed-dose combination ARB/diuretic	63.9 % (535/837)	65.9 % (211/320)	63.6 % (239/376)	60.3 % (85/141)	0.49811
Fixed-dose combination ARB/calcium channel blocker	38.7 % (180/465)	38.8 % (69/178)	40.4 % (86/213)	33.8 % (25/74)	0.60466
Fixed-dose combination ACE inhibitor/calcium channel blocker	13.9 % (137/983)	15.0 % (54/360)	12.2 % (52/425)	15.7 % (31/198)	0.39587
Fixed-dose combination direct renin inhibitor/diuretic	52.6 % (10/19)	37.5 % (3/8)	62.5 % (5/8)	66.7 % (2/3)	0.52617
Novartis drugs					
Valsartan / Hydrochlorothiazide					
CoDiovan	30.2 % (57/189)	32.9 % (24/73)	33.7 % (30/89)	11.1 % (3/27)	0.06591
Codiovan forte	14.3 % (27/189)	15.1 % (11/73)	14.6 % (13/89)	11.1 % (3/27)	0.87536
Cordinate plus	1.6 % (3/189)	2.7 % (2/73)	0.0 % (0/89)	3.7 % (1/27)	0.24289
Provas	0.5 % (1/189)	0.0 % (0/73)	1.1 % (1/89)	0.0 % (0/27)	0.56848
Provas comp	5.8 % (11/189)	5.5 % (4/73)	5.6 % (5/89)	7.4 % (2/27)	0.92951
Provas maxx	1.6 % (3/189)	1.4 % (1/73)	2.2 % (2/89)	0.0 % (0/27)	0.70269
Other	46.0 % (87/189)	42.5 % (31/73)	42.7 % (38/89)	66.7 % (18/27)	0.06721
Valsartan					
Cordinate	3.3 % (10/300)	2.4 % (3/127)	3.8 % (5/133)	5.0 % (2/40)	0.67319
Diovan	33.3 % (100/300)	33.9 % (43/127)	31.6 % (42/133)	37.5 % (15/40)	0.77396
Provas	6.7 % (20/300)	5.5 % (7/127)	7.5 % (10/133)	7.5 % (3/40)	0.78975
Other	56.7 % (170/300)	58.3 % (74/127)	57.1 % (76/133)	50.0 % (20/40)	0.64764
Valsartan / Amlodipine / Hydrochlorothiazide					
Exforge HCT	76.8 % (159/207)	81.0 % (64/79)	78.4 % (69/88)	65.0 % (26/40)	0.13252
Dafiro HCT	12.6 % (26/207)	8.9 % (7/79)	13.6 % (12/88)	17.5 % (7/40)	0.37419
Other	10.6 % (22/207)	10.1 % (8/79)	8.0 % (7/88)	17.5 % (7/40)	0.26292
Aliskiren					
Rasilez	95.0 % (19/20)	100.0 % (12/12)	100.0 % (6/6)	50.0 % (1/2)	0.00877
Other	5.0 % (1/20)	0.0 % (0/12)	0.0 % (0/6)	50.0 % (1/2)	0.00877
Hydrochlorothiazide					
Esidrix	4.0 % (22/553)	5.0 % (11/221)	3.6 % (8/224)	2.8 % (3/108)	0.58216
Other	96.0 % (531/553)	95.0 % (210/221)	96.4 % (216/224)	97.2 % (105/108)	0.58216
Aliskiren / Hydrochlorothiazide					

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
Rasilez HCT	90.0 % (9/10)	66.7 % (2/3)	100.0 % (5/5)	100.0 % (2/2)	0.27354
Other	10.0 % (1/10)	33.3 % (1/3)	0.0 % (0/5)	0.0 % (0/2)	0.27354
Valsartan / Amlodipine					
Exforge	81.4 % (83/102)	75.0 % (24/32)	82.7 % (43/52)	88.9 % (16/18)	0.45204
Dafiro	15.7 % (16/102)	21.9 % (7/32)	13.5 % (7/52)	11.1 % (2/18)	0.49505
Other	2.9 % (3/102)	3.1 % (1/32)	3.8 % (2/52)	0.0 % (0/18)	0.70524

Table 9-51. *Hypoglycemic events in the HbA1c treatment groups at 6-month follow-up.*

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
No. of patients with FU data	7355 (100.0 %)	2886 (39.2 %)	3197 (43.5 %)	1272 (17.3 %)	
Hypoglycemic events since baseline					
Without specific symptoms	0.3 % (25/7155)	0.3 % (8/2821)	0.4 % (12/3122)	0.4 % (5/1212)	0.74106
No. of events	2.28 ± 1.65, n=25	1.75 ± 1.39, n=8	2.58 ± 2.07, n=12	2.40 ± 0.55, n=5	0.18182
Symptomatic, but controllable without external help	0.4 % (26/7211)	0.2 % (6/2845)	0.4 % (14/3137)	0.5 % (6/1229)	0.22618
No. of events	2.46 ± 3.02, n=26	2.50 ± 1.76, n=6	2.86 ± 3.94, n=14	1.50 ± 0.84, n=6	0.57626
External help needed	0.0 % (2/7220)	0.0 % (0/2850)	0.0 % (1/3139)	0.1 % (1/1231)	0.35289
No. of events	1.00 ± 0.00, n=2	, n=0	1.00, n=1	1.00, n=1	
Symptomatic with medical help	0.0 % (1/7219)	0.0 % (1/2848)	0.0 % (0/3140)	0.0 % (0/1231)	0.46418
No. of events	1.00, n=1	1.00, n=1	, n=0	, n=0	
Hospitalization required	0.0 % (1/7228)	0.0 % (0/2852)	0.0 % (0/3143)	0.1 % (1/1233)	0.08791
No. of events	1.00, n=1	, n=0	, n=0	1.00, n=1	

Therapeutic patterns at 12 months follow-up

Table 9-52 shows anti-diabetic therapy in the in the HbA1c treatment groups at 12-month follow-up (i.e. Metformin; Sulfonylurea drugs; Glucosidase inhibitors; Glinide; Glitazone; DPP-4 inhibitors; GLP-1 analogs; SGTL-2 inhibitors; Total number of antidiabetics; Insulin; Novartis drugs).

Table 9-53 shows anti-hypertensive therapy in the in the HbA1c treatment groups at 12-month follow-up (i.e. ACE inhibitors; ARB; Direct renin inhibitor; Beta-blocker; Calcium channel blocker; Diuretic drugs; Total number of antihypertensive drugs; Fixed-dose combinations; Novartis drugs).

Table 9-54 shows hypoglycemic events in the in the HbA1c treatment groups at 12-month follow-up (i.e. Number of events; Type of events; Help needed).

Table 9-52. *Antidiabetic therapy in the HbA1c treatment groups at 12-month follow-up.*

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
No. of patients with FU data	6691 (100.0 %)	2644 (39.5 %)	2912 (43.5 %)	1135 (17.0 %)	
Metformin	79.8 % (5338/6691)	78.9 % (2086/2644)	80.7 % (2349/2912)	79.6 % (903/1135)	0.25490
Metformin, dosage [mg/day]	1737.07 ± 515.80, n=5338	1654.01 ± 537.82, n=2086	1796.21 ± 492.79, n=2349	1775.12 ± 496.92, n=903	<.00001
Sulfonylurea drugs	17.6 % (1176/6689)	15.1 % (400/2644)	18.4 % (535/2911)	21.3 % (241/1134)	0.00001
Sulfonylurea drugs, dosage [mg/day]	3.17 ± 1.91, n=1176	3.02 ± 1.96, n=400	3.25 ± 1.86, n=535	3.25 ± 1.94, n=241	0.01678
Substance					
Carbutamide	0.0 % (0/1176)	0.0 % (0/400)	0.0 % (0/535)	0.0 % (0/241)	
Tolbutamide	0.0 % (0/1176)	0.0 % (0/400)	0.0 % (0/535)	0.0 % (0/241)	
Glibenclamide	18.8 % (221/1176)	22.5 % (90/400)	17.4 % (93/535)	15.8 % (38/241)	0.05658
Glibornuride	0.0 % (0/1176)	0.0 % (0/400)	0.0 % (0/535)	0.0 % (0/241)	
Gliclazide	0.0 % (0/1176)	0.0 % (0/400)	0.0 % (0/535)	0.0 % (0/241)	
Glipizide	0.0 % (0/1176)	0.0 % (0/400)	0.0 % (0/535)	0.0 % (0/241)	
Gliquidone	0.4 % (5/1176)	0.5 % (2/400)	0.4 % (2/535)	0.4 % (1/241)	0.95752
Glisoxepide	0.0 % (0/1176)	0.0 % (0/400)	0.0 % (0/535)	0.0 % (0/241)	
Glycodiazine	0.5 % (6/1176)	0.5 % (2/400)	0.4 % (2/535)	0.8 % (2/241)	0.71105
Glimepiride	79.8 % (938/1176)	76.3 % (305/400)	81.3 % (435/535)	82.2 % (198/241)	0.09509
Other	0.5 % (6/1176)	0.3 % (1/400)	0.6 % (3/535)	0.8 % (2/241)	0.59285
Glucosidase inhibitors	1.2 % (78/6690)	1.1 % (28/2644)	1.4 % (41/2912)	0.8 % (9/1134)	0.21155
Glucosidase inhibitors, dosage [mg/day]	148.42 ± 79.73, n=78	107.75 ± 43.10, n=28	170.98 ± 89.66, n=41	172.22 ± 75.46, n=9	0.00413
Substance					
Acarbose	92.3 % (72/78)	85.7 % (24/28)	95.1 % (39/41)	100.0 % (9/9)	0.23205
Miglitol	6.4 % (5/78)	14.3 % (4/28)	2.4 % (1/41)	0.0 % (0/9)	0.10082

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
Other	1.3 % (1/78)	0.0 % (0/28)	2.4 % (1/41)	0.0 % (0/9)	0.63313
Glinide	4.0 % (265/6690)	2.9 % (76/2644)	4.1 % (119/2912)	6.2 % (70/1134)	0.00001
Glinide, dosage [mg/day]	14.78 ± 58.56, n=265	11.50 ± 44.47, n=76	16.96 ± 65.13, n=119	14.62 ± 60.81, n=70	0.91213
Substance					
Nateglinide	3.4 % (9/265)	2.6 % (2/76)	4.2 % (5/119)	2.9 % (2/70)	0.80543
Repaglinide	94.3 % (250/265)	96.1 % (73/76)	92.4 % (110/119)	95.7 % (67/70)	0.47901
Other	2.3 % (6/265)	1.3 % (1/76)	3.4 % (4/119)	1.4 % (1/70)	0.55513
Glitazone	0.5 % (34/6690)	0.5 % (13/2644)	0.7 % (19/2912)	0.2 % (2/1134)	0.15862
Glitazone, dosage [mg/day]	39.44 ± 22.67, n=34	30.38 ± 11.27, n=13	48.95 ± 24.24, n=19	8.00 ± 9.90, n=2	0.00363
Substance					
Pioglitazon	85.3 % (29/34)	100.0 % (13/13)	73.7 % (14/19)	100.0 % (2/2)	0.09887
Other	14.7 % (5/34)	0.0 % (0/13)	26.3 % (5/19)	0.0 % (0/2)	0.09887
DPP-4 inhibitors	61.9 % (4140/6691)	58.9 % (1557/2644)	64.6 % (1881/2912)	61.9 % (702/1135)	0.00007
DPP-4 inhibitors, dosage [mg/day]	84.52 ± 31.33, n=4140	84.13 ± 33.46, n=1557	84.44 ± 29.01, n=1881	85.59 ± 32.44, n=702	0.06882
Substance					
Sitagliptin	31.7 % (1312/4140)	30.4 % (473/1557)	32.1 % (603/1881)	33.6 % (236/702)	0.27813
Vildagliptin	63.0 % (2607/4140)	64.9 % (1011/1557)	62.4 % (1173/1881)	60.3 % (423/702)	0.07853
Linagliptin	0.0 % (0/4140)	0.0 % (0/1557)	0.0 % (0/1881)	0.0 % (0/702)	
Saxagliptin	5.0 % (208/4140)	4.3 % (67/1557)	5.4 % (101/1881)	5.7 % (40/702)	0.24240
Other	0.3 % (13/4140)	0.4 % (6/1557)	0.2 % (4/1881)	0.4 % (3/702)	0.56028
GLP-1 analogs/mimetics	5.1 % (343/6690)	4.4 % (116/2644)	5.8 % (168/2912)	5.2 % (59/1134)	0.06532
GLP-1 analogs/mimetics, dosage [mg/day]	7.15 ± 14.01, n=343	7.12 ± 12.96, n=116	7.52 ± 14.95, n=168	6.15 ± 13.40, n=59	0.47092
Substance					
Exenatide	39.4 % (135/343)	37.9 % (44/116)	38.7 % (65/168)	44.1 % (26/59)	0.71225
Liraglutide	54.5 % (187/343)	51.7 % (60/116)	57.7 % (97/168)	50.8 % (30/59)	0.49950

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
Other	6.1 % (21/343)	10.3 % (12/116)	3.6 % (6/168)	5.1 % (3/59)	0.06048
SGTL-2 inhibitors	2.5 % (170/6690)	2.2 % (59/2644)	2.5 % (74/2912)	3.3 % (37/1134)	0.18192
SGTL-2 inhibitors, dosage [mg/day]	11.98 ± 14.11, n=170	12.80 ± 16.51, n=59	12.72 ± 15.41, n=74	9.19 ± 1.87, n=37	0.04648
Substance					
Dapagliflozin	95.9 % (163/170)	96.6 % (57/59)	94.6 % (70/74)	97.3 % (36/37)	0.74916
Other	4.1 % (7/170)	3.4 % (2/59)	5.4 % (4/74)	2.7 % (1/37)	0.74916
Insulin(rapid-acting or long-acting or Pre-mixed)	19.6 % (1313/6691)	13.8 % (364/2644)	21.9 % (637/2912)	27.5 % (312/1135)	<.00001
Rapid-acting insulin	6.9 % (463/6690)	5.3 % (141/2644)	7.0 % (205/2912)	10.3 % (117/1134)	<.00001
Human insulin	43.0 % (199/463)	47.5 % (67/141)	40.0 % (82/205)	42.7 % (50/117)	0.38091
Analogues	57.0 % (264/463)	52.5 % (74/141)	60.0 % (123/205)	57.3 % (67/117)	0.38091
Syringe	3.7 % (17/463)	1.4 % (2/141)	3.4 % (7/205)	6.8 % (8/117)	0.06795
Pen	96.3 % (446/463)	98.6 % (139/141)	96.6 % (198/205)	93.2 % (109/117)	0.06795
Pump	0.0 % (0/463)	0.0 % (0/141)	0.0 % (0/205)	0.0 % (0/117)	
Other	0.0 % (0/463)	0.0 % (0/141)	0.0 % (0/205)	0.0 % (0/117)	
U-40	15.4 % (71/461)	19.1 % (27/141)	12.7 % (26/204)	15.5 % (18/116)	0.26904
U-100	84.6 % (390/461)	80.9 % (114/141)	87.3 % (178/204)	84.5 % (98/116)	0.26904
1x insulin/day	9.3 % (43/463)	12.1 % (17/141)	6.3 % (13/205)	11.1 % (13/117)	0.14535
2x insulin/day	13.4 % (62/463)	16.3 % (23/141)	12.2 % (25/205)	12.0 % (14/117)	0.47354
3x insulin/day	76.0 % (352/463)	70.9 % (100/141)	80.5 % (165/205)	74.4 % (87/117)	0.10900
4x insulin/day	1.3 % (6/463)	0.7 % (1/141)	1.0 % (2/205)	2.6 % (3/117)	0.36513
Long-acting insulin	18.3 % (1225/6690)	12.6 % (334/2644)	20.6 % (601/2912)	25.6 % (290/1134)	<.00001
Human insulin	29.3 % (359/1225)	32.6 % (109/334)	26.8 % (161/601)	30.7 % (89/290)	0.14280

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
Analogues	70.7 % (866/1225)	67.4 % (225/334)	73.2 % (440/601)	69.3 % (201/290)	0.14280
Syringe	5.8 % (71/1225)	6.0 % (20/334)	5.2 % (31/601)	6.9 % (20/290)	0.57298
Pen	93.9 % (1150/1225)	93.7 % (313/334)	94.3 % (567/601)	93.1 % (270/290)	0.76168
Pump	0.2 % (2/1225)	0.0 % (0/334)	0.3 % (2/601)	0.0 % (0/290)	0.35347
Other	0.2 % (2/1225)	0.3 % (1/334)	0.2 % (1/601)	0.0 % (0/290)	0.65235
U-40	15.3 % (187/1221)	18.3 % (61/333)	11.8 % (71/600)	19.1 % (55/288)	0.00389
U-100	84.7 % (1034/1221)	81.7 % (272/333)	88.2 % (529/600)	80.9 % (233/288)	0.00389
1x insulin/day	86.2 % (1056/1225)	84.1 % (281/334)	86.9 % (522/601)	87.2 % (253/290)	0.43111
2x insulin/day	12.2 % (150/1225)	12.6 % (42/334)	12.1 % (73/601)	12.1 % (35/290)	0.97647
3x insulin/day	1.5 % (18/1225)	3.0 % (10/334)	1.0 % (6/601)	0.7 % (2/290)	0.02350
4x insulin/day	0.1 % (1/1225)	0.3 % (1/334)	0.0 % (0/601)	0.0 % (0/290)	0.26318
Pre-mixed insulin	2.3 % (154/6690)	1.1 % (30/2644)	2.8 % (82/2912)	3.7 % (42/1134)	<.00001
Human insulin	65.6 % (101/154)	66.7 % (20/30)	65.9 % (54/82)	64.3 % (27/42)	0.97551
Analogues	34.4 % (53/154)	33.3 % (10/30)	34.1 % (28/82)	35.7 % (15/42)	0.97551
Syringe	5.2 % (8/153)	0.0 % (0/30)	3.7 % (3/81)	11.9 % (5/42)	0.05467
Pen	94.8 % (145/153)	100.0 % (30/30)	96.3 % (78/81)	88.1 % (37/42)	0.05467
Pump	0.0 % (0/153)	0.0 % (0/30)	0.0 % (0/81)	0.0 % (0/42)	
Other	0.0 % (0/153)	0.0 % (0/30)	0.0 % (0/81)	0.0 % (0/42)	
U-40	15.8 % (24/152)	20.0 % (6/30)	12.5 % (10/80)	19.0 % (8/42)	0.49998
U-100	84.2 % (128/152)	80.0 % (24/30)	87.5 % (70/80)	81.0 % (34/42)	0.49998
1x insulin/day	10.5 % (16/153)	6.7 % (2/30)	8.6 % (7/81)	16.7 % (7/42)	0.29014

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
2x insulin/day	84.3 % (129/153)	90.0 % (27/30)	87.7 % (71/81)	73.8 % (31/42)	0.08540
3x insulin/day	4.6 % (7/153)	3.3 % (1/30)	2.5 % (2/81)	9.5 % (4/42)	0.19352
4x insulin/day	0.7 % (1/153)	0.0 % (0/30)	1.2 % (1/81)	0.0 % (0/42)	0.63931
Fixed-dose combination metformin / DPP-4 inhibitor	78.1 % (2644/3385)	78.3 % (965/1232)	77.3 % (1203/1557)	79.9 % (476/596)	0.41467
Novartis drugs					
Vildagliptin / Metformin					
Eucreas	91.8 % (1630/1776)	92.3 % (601/651)	91.5 % (752/822)	91.4 % (277/303)	0.81923
Icandra	8.2 % (146/1776)	7.7 % (50/651)	8.5 % (70/822)	8.6 % (26/303)	0.81923
Vildagliptin					
Galvus	85.1 % (707/831)	82.5 % (297/360)	88.0 % (309/351)	84.2 % (101/120)	0.11195
Jalra	14.9 % (124/831)	17.5 % (63/360)	12.0 % (42/351)	15.8 % (19/120)	0.11195
Nateglinide					
STARLIX	100.0 % (9/9)	100.0 % (2/2)	100.0 % (5/5)	100.0 % (2/2)	
Other	0.0 % (0/9)	0.0 % (0/2)	0.0 % (0/5)	0.0 % (0/2)	

Table 9-53. *Anti-hypertensive therapy in the HbA1c treatment groups at 12-month follow-up.*

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
No. of patients with FU data	6691 (100.0 %)	2644 (39.5 %)	2912 (43.5 %)	1135 (17.0 %)	
ACE inhibitors	52.1 % (3483/6690)	50.7 % (1340/2644)	53.6 % (1560/2911)	51.4 % (583/1135)	0.08356
ACE inhibitors, dosage [mg/day]	10.0 (5.0, 10.0)	7.5 (5.0, 10.0)	8.8 (5.0, 10.0)	10.0 (5.0, 10.0)	0.06495
Substance					
Captopril	2.4 % (83/3483)	2.8 % (38/1340)	2.1 % (33/1560)	2.1 % (12/583)	0.38181
Enalapril	17.7 % (616/3483)	19.3 % (259/1340)	16.1 % (251/1560)	18.2 % (106/583)	0.07024
Lisinopril	11.8 % (411/3483)	11.8 % (158/1340)	12.1 % (188/1560)	11.1 % (65/583)	0.84706
Ramipril	65.0 % (2264/3483)	63.2 % (847/1340)	66.8 % (1042/1560)	64.3 % (375/583)	0.12147
Trandolapril	0.2 % (6/3483)	0.1 % (2/1340)	0.1 % (2/1560)	0.3 % (2/583)	0.54711
Other	3.0 % (103/3483)	2.7 % (36/1340)	2.8 % (44/1560)	3.9 % (23/583)	0.29727
Angiotensin receptor blocker (ARB)	28.8 % (1929/6690)	28.8 % (762/2644)	29.6 % (863/2911)	26.8 % (304/1135)	0.19591
ARB, dosage [mg/day]	80.0 (20.0, 160.0)	80.0 (32.0, 160.0)	80.0 (20.0, 160.0)	80.0 (32.0, 160.0)	0.16947
Substance					
Candesartan	23.1 % (446/1929)	22.2 % (169/762)	23.1 % (199/863)	25.7 % (78/304)	0.47631
Irbesartan	5.5 % (107/1929)	6.2 % (47/762)	5.2 % (45/863)	4.9 % (15/304)	0.61848
Losartan	7.3 % (141/1929)	7.2 % (55/762)	6.7 % (58/863)	9.2 % (28/304)	0.35478
Valsartan	39.8 % (768/1929)	39.5 % (301/762)	40.2 % (347/863)	39.5 % (120/304)	0.95035
Other	24.2 % (467/1929)	24.9 % (190/762)	24.8 % (214/863)	20.7 % (63/304)	0.30212
Direct renin inhibitor	0.4 % (26/6690)	0.5 % (13/2644)	0.3 % (10/2911)	0.3 % (3/1135)	0.51393
Direct renin inhibitor, dosage [mg/day]	150.0 (150.0, 300.0)	150.0 (150.0, 150.0)	300.0 (150.0, 300.0)	150.0 (150.0, 300.0)	0.07189
Beta-blocker	48.7 % (3256/6690)	47.8 % (1263/2644)	49.4 % (1439/2911)	48.8 % (554/1135)	0.46123
Beta-blocker, dosage [mg/day]	25.0 (5.0, 95.0)	15.0 (5.0, 95.0)	25.0 (5.0, 95.0)	10.0 (5.0, 95.0)	0.00323
Substance					
Metoprolol	45.0 % (1464/3256)	44.3 % (560/1263)	47.0 % (677/1439)	41.0 % (227/554)	0.04319
Bisoprolol	41.5 % (1350/3256)	42.6 % (538/1263)	39.0 % (561/1439)	45.3 % (251/554)	0.02148

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
Nebivolol	5.5 % (180/3256)	5.9 % (75/1263)	5.0 % (72/1439)	6.0 % (33/554)	0.50662
Carvedilol	4.7 % (152/3256)	4.0 % (51/1263)	5.4 % (78/1439)	4.2 % (23/554)	0.19312
Other	3.4 % (110/3256)	3.1 % (39/1263)	3.5 % (51/1439)	3.6 % (20/554)	0.76386
Calcium channel blocker	29.1 % (1950/6690)	27.6 % (731/2644)	29.8 % (867/2911)	31.0 % (352/1135)	0.06843
Calcium channel blocker, dosage [mg/day]	10.0 (5.0, 10.0)	10.0 (5.0, 10.0)	10.0 (5.0, 10.0)	10.0 (5.0, 10.0)	0.33985
Substance					
Amlodipine	75.1 % (1465/1950)	73.5 % (537/731)	76.5 % (663/867)	75.3 % (265/352)	0.38135
Nifedipine	2.2 % (42/1950)	2.3 % (17/731)	2.0 % (17/867)	2.3 % (8/352)	0.86969
Nisoldipine	0.1 % (1/1950)	0.0 % (0/731)	0.1 % (1/867)	0.0 % (0/352)	0.53532
Nimodipine	0.1 % (1/1950)	0.1 % (1/731)	0.0 % (0/867)	0.0 % (0/352)	0.43421
Diltiazem	0.6 % (12/1950)	0.5 % (4/731)	0.3 % (3/867)	1.4 % (5/352)	0.09007
Verapamil	3.3 % (64/1950)	2.7 % (20/731)	3.5 % (30/867)	4.0 % (14/352)	0.51961
Gallopamil	0.0 % (0/1950)	0.0 % (0/731)	0.0 % (0/867)	0.0 % (0/352)	
Felodipine	3.0 % (58/1950)	2.5 % (18/731)	3.5 % (30/867)	2.8 % (10/352)	0.49787
Nitrendipine	4.2 % (81/1950)	4.4 % (32/731)	4.7 % (41/867)	2.3 % (8/352)	0.13940
Lercanidipine	10.5 % (204/1950)	12.9 % (94/731)	8.1 % (70/867)	11.4 % (40/352)	0.00651
Nilvadipine	0.1 % (1/1950)	0.0 % (0/731)	0.1 % (1/867)	0.0 % (0/352)	0.53532
Manidipine	0.1 % (1/1950)	0.1 % (1/731)	0.0 % (0/867)	0.0 % (0/352)	0.43421
Isradipine	0.1 % (2/1950)	0.3 % (2/731)	0.0 % (0/867)	0.0 % (0/352)	0.18838
Other	0.9 % (18/1950)	0.7 % (5/731)	1.3 % (11/867)	0.6 % (2/352)	0.35445
Diuretic drugs	44.2 % (2954/6690)	41.9 % (1108/2644)	45.1 % (1314/2911)	46.9 % (532/1135)	0.00686
Diuretic drugs, dosage [mg/day]	20.0 (12.5, 25.0)	18.1 (12.5, 25.0)	20.0 (12.5, 25.0)	14.3 (12.5, 25.0)	0.71204
Substance					
Furosemide	8.4 % (248/2954)	6.7 % (74/1108)	9.7 % (127/1314)	8.8 % (47/532)	0.02824
Torasemide	23.3 % (688/2954)	22.6 % (250/1108)	22.8 % (300/1314)	25.9 % (138/532)	0.27618
Bumetanide	0.0 % (1/2954)	0.0 % (0/1108)	0.1 % (1/1314)	0.0 % (0/532)	0.53566
Etacrynic acid	0.0 % (1/2954)	0.0 % (0/1108)	0.1 % (1/1314)	0.0 % (0/532)	0.53566
Piretanide	1.1 % (32/2954)	1.4 % (15/1108)	0.9 % (12/1314)	0.9 % (5/532)	0.54516
Hydrochlorothiazide	69.7 % (2059/2954)	72.4 % (802/1108)	68.8 % (904/1314)	66.4 % (353/532)	0.02867

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
Clopamid	0.2 % (7/2954)	0.2 % (2/1108)	0.2 % (3/1314)	0.4 % (2/532)	0.74520
Other	8.5 % (250/2954)	7.2 % (80/1108)	9.0 % (118/1314)	9.8 % (52/532)	0.14632
Other anti-hypertensive therapy	10.8 % (723/6690)	9.5 % (250/2644)	11.2 % (327/2911)	12.9 % (146/1135)	0.00515
Fixed-dose combinations					
Fixed-dose combination ARB/calcium channel blocker/diuretic	72.8 % (422/580)	71.1 % (160/225)	73.6 % (190/258)	74.2 % (72/97)	0.77278
Fixed-dose combination ACE inhibitor/diuretic	50.0 % (741/1483)	51.6 % (286/554)	49.2 % (324/659)	48.5 % (131/270)	0.60507
Fixed-dose combination ARB/diuretic	64.9 % (504/776)	67.5 % (204/302)	64.2 % (221/344)	60.8 % (79/130)	0.37345
Fixed-dose combination ARB/calcium channel blocker	39.6 % (170/429)	38.9 % (65/167)	41.0 % (82/200)	37.1 % (23/62)	0.83603
Fixed-dose combination ACE inhibitor/calcium channel blocker	16.0 % (146/914)	17.4 % (58/334)	14.0 % (55/394)	17.7 % (33/186)	0.34885
Fixed-dose combination direct renin inhibitor/diuretic	50.0 % (8/16)	33.3 % (2/6)	57.1 % (4/7)	66.7 % (2/3)	0.56472
Novartis drugs					
Valsartan / Hydrochlorothiazide					
CoDiovan	31.4 % (54/172)	36.8 % (25/68)	34.2 % (27/79)	8.0 % (2/25)	0.02297
Codiovan forte	13.4 % (23/172)	16.2 % (11/68)	13.9 % (11/79)	4.0 % (1/25)	0.30451
Cordinate plus	1.7 % (3/172)	2.9 % (2/68)	0.0 % (0/79)	4.0 % (1/25)	0.25753
Provas	0.6 % (1/172)	0.0 % (0/68)	1.3 % (1/79)	0.0 % (0/25)	0.55319
Provas comp	5.2 % (9/172)	5.9 % (4/68)	3.8 % (3/79)	8.0 % (2/25)	0.67973
Provas maxx	1.7 % (3/172)	1.5 % (1/68)	2.5 % (2/79)	0.0 % (0/25)	0.68409
Other	45.9 % (79/172)	36.8 % (25/68)	44.3 % (35/79)	76.0 % (19/25)	0.00320
Valsartan					
Cordinate	1.5 % (4/261)	1.9 % (2/104)	0.0 % (0/120)	5.4 % (2/37)	0.05930
Diovan	27.6 % (72/261)	26.0 % (27/104)	28.3 % (34/120)	29.7 % (11/37)	0.87983
Provas	7.3 % (19/261)	6.7 % (7/104)	7.5 % (9/120)	8.1 % (3/37)	0.95472
Other	63.6 % (166/261)	65.4 % (68/104)	64.2 % (77/120)	56.8 % (21/37)	0.63502
Valsartan / Amlodipine / Hydrochlorothiazide					
Exforge HCT	76.2 % (160/210)	80.0 % (68/85)	74.7 % (65/87)	71.1 % (27/38)	0.51230
Dafiro HCT	13.3 % (28/210)	9.4 % (8/85)	14.9 % (13/87)	18.4 % (7/38)	0.33665
Other	10.5 % (22/210)	10.6 % (9/85)	10.3 % (9/87)	10.5 % (4/38)	0.99858
Aliskiren					

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
Rasilez	100.0 % (18/18)	100.0 % (11/11)	100.0 % (6/6)	100.0 % (1/1)	
Other	0.0 % (0/18)	0.0 % (0/11)	0.0 % (0/6)	0.0 % (0/1)	
Hydrochlorothiazide					
Esidrix	4.3 % (22/512)	5.0 % (10/201)	4.1 % (9/219)	3.3 % (3/92)	0.78519
Other	95.7 % (490/512)	95.0 % (191/201)	95.9 % (210/219)	96.7 % (89/92)	0.78519
Aliskiren / Hydrochlorothiazide					
Rasilez HCT	87.5 % (7/8)	50.0 % (1/2)	100.0 % (4/4)	100.0 % (2/2)	0.18009
Other	12.5 % (1/8)	50.0 % (1/2)	0.0 % (0/4)	0.0 % (0/2)	0.18009
Valsartan / Amlodipine					
Exforge	86.6 % (84/97)	81.8 % (27/33)	85.4 % (41/48)	100.0 % (16/16)	0.20357
Dafiro	10.3 % (10/97)	15.2 % (5/33)	10.4 % (5/48)	0.0 % (0/16)	0.26230
Other	3.1 % (3/97)	3.0 % (1/33)	4.2 % (2/48)	0.0 % (0/16)	0.70618

Table 9-54. *Hypoglycemic events in the HbA1c treatment groups at 12-month follow-up.*

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
No. of patients with FU data	6691 (100.0 %)	2644 (39.5 %)	2912 (43.5 %)	1135 (17.0 %)	
Hypoglycemic events since last FU					
Without specific symptoms	0.2 % (10/6480)	0.0 % (1/2577)	0.3 % (8/2824)	0.1 % (1/1079)	0.06247
No. of events	2.30 ± 1.89, n=10	1.00, n=1	2.63 ± 2.00, n=8	1.00, n=1	0.24745
Symptomatic, but controllable without external help	0.1 % (9/6557)	0.1 % (2/2598)	0.1 % (4/2862)	0.3 % (3/1097)	0.33707
No. of events	2.00 ± 1.32, n=9	2.00 ± 1.41, n=2	2.50 ± 1.73, n=4	1.33 ± 0.58, n=3	0.52567
External help needed	0.0 % (0/6557)	0.0 % (0/2596)	0.0 % (0/2863)	0.0 % (0/1098)	
No. of events	, n=0	, n=0	, n=0	, n=0	
Symptomatic with medical help	0.0 % (1/6568)	0.0 % (0/2602)	0.0 % (1/2867)	0.0 % (0/1099)	0.52438
No. of events	1.00, n=1	, n=0	1.00, n=1	, n=0	
Hospitalization required	0.0 % (2/6572)	0.0 % (0/2603)	0.0 % (1/2869)	0.1 % (1/1100)	0.34416
No. of events	1.00 ± 0.00, n=2	, n=0	1.00, n=1	1.00, n=1	

Therapeutic patterns at 24 months follow-up

Table 9-55 shows anti-diabetic therapy in the in the HbA1c treatment groups at 24-month follow-up (i.e. Metformin; Sulfonylurea drugs; Glucosidase inhibitors; Glinide; Glitazone; DPP-4 inhibitors; GLP-1 analogs; SGTL-2 inhibitors; Total number of antidiabetics; Insulin; Novartis drugs).

Table 9-56 shows anti-hypertensive therapy in the in the HbA1c treatment groups at 24-month follow-up (i.e. ACE inhibitors; ARB; Direct renin inhibitor; Beta-blocker; Calcium channel blocker; Diuretic drugs; Total number of antihypertensive drugs; Fixed-dose combinations; Novartis drugs).

Table 9-57 shows hypoglycemic events in the in the HbA1c treatment groups at 24-month follow-up (i.e. Number of events; Type of events; Help needed).

Table 9-55. *Antidiabetic therapy in the HbA1c treatment groups at 24-month follow-up.*

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
No. of patients with FU data	4130 (100.0 %)	1671 (40.5 %)	1808 (43.8 %)	651 (15.8 %)	
Metformin	79.6 % (3286/4130)	77.8 % (1300/1671)	80.9 % (1463/1808)	80.3 % (523/651)	0.06441
Metformin, dosage [mg/day]	1740.70 ± 505.41, n=3286	1661.28 ± 524.68, n=1300	1790.40 ± 492.23, n=1463	1799.06 ± 466.69, n=523	<.00001
Sulfonylurea drugs	18.0 % (744/4130)	16.6 % (277/1671)	18.3 % (331/1808)	20.9 % (136/651)	0.04759
Sulfonylurea drugs, dosage [mg/day]	3.18 ± 1.86, n=744	3.06 ± 1.95, n=277	3.29 ± 1.80, n=331	3.14 ± 1.79, n=136	0.04205
Substance					
Carbutamide	0.0 % (0/744)	0.0 % (0/277)	0.0 % (0/331)	0.0 % (0/136)	
Tolbutamide	0.0 % (0/744)	0.0 % (0/277)	0.0 % (0/331)	0.0 % (0/136)	
Glibenclamide	19.9 % (148/744)	23.8 % (66/277)	18.7 % (62/331)	14.7 % (20/136)	0.07184
Glibornuride	0.0 % (0/744)	0.0 % (0/277)	0.0 % (0/331)	0.0 % (0/136)	
Gliclazide	0.0 % (0/744)	0.0 % (0/277)	0.0 % (0/331)	0.0 % (0/136)	
Glipizide	0.0 % (0/744)	0.0 % (0/277)	0.0 % (0/331)	0.0 % (0/136)	
Gliquidone	0.4 % (3/744)	0.4 % (1/277)	0.6 % (2/331)	0.0 % (0/136)	0.63894
Glisoxepide	0.0 % (0/744)	0.0 % (0/277)	0.0 % (0/331)	0.0 % (0/136)	
Glycodiazine	0.3 % (2/744)	0.0 % (0/277)	0.6 % (2/331)	0.0 % (0/136)	0.28619
Glimepiride	79.0 % (588/744)	75.5 % (209/277)	79.8 % (264/331)	84.6 % (115/136)	0.09276
Other	0.4 % (3/744)	0.4 % (1/277)	0.3 % (1/331)	0.7 % (1/136)	0.79058
Glucosidase inhibitors	1.2 % (49/4130)	1.4 % (23/1671)	1.2 % (22/1808)	0.6 % (4/651)	0.30952
Glucosidase inhibitors, dosage [mg/day]	121.12 ± 61.50, n=49	105.43 ± 42.45, n=23	132.27 ± 67.33, n=22	150.00 ± 108.01, n=4	0.28574
Substance					
Acarbose	87.8 % (43/49)	78.3 % (18/23)	95.5 % (21/22)	100.0 % (4/4)	0.15714
Miglitol	10.2 % (5/49)	17.4 % (4/23)	4.5 % (1/22)	0.0 % (0/4)	0.28366
Other	2.0 % (1/49)	4.3 % (1/23)	0.0 % (0/22)	0.0 % (0/4)	0.56158
Glinide	3.7 % (152/4130)	2.4 % (40/1671)	3.6 % (65/1808)	7.2 % (47/651)	<.00001
Glinide, dosage [mg/day]	8.42 ± 36.30, n=152	6.08 ± 18.57, n=40	10.34 ± 45.03, n=65	7.78 ± 34.67, n=47	0.31291
Substance					
Nateglinide	2.6 % (4/152)	2.5 % (1/40)	3.1 % (2/65)	2.1 % (1/47)	0.95142
Repaglinide	94.7 % (144/152)	97.5 % (39/40)	90.8 % (59/65)	97.9 % (46/47)	0.16602
Other	2.6 % (4/152)	0.0 % (0/40)	6.2 % (4/65)	0.0 % (0/47)	0.06397
Glitazone	0.7 % (28/4130)	0.7 % (11/1671)	0.9 % (16/1808)	0.2 % (1/651)	0.14822

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
Glitazone, dosage [mg/day]	38.79 ± 21.65, n=28	28.64 ± 12.06, n=11	48.13 ± 21.98, n=16	1.00, n=1	0.00828
Substance					
Pioglitazon	82.1 % (23/28)	90.9 % (10/11)	75.0 % (12/16)	100.0 % (1/1)	0.50911
Other	17.9 % (5/28)	9.1 % (1/11)	25.0 % (4/16)	0.0 % (0/1)	0.50911
DPP-4 inhibitors	59.8 % (2469/4130)	56.9 % (951/1671)	61.3 % (1108/1808)	63.0 % (410/651)	0.00613
DPP-4 inhibitors, dosage [mg/day]	83.43 ± 34.32, n=2469	83.96 ± 38.01, n=951	82.24 ± 32.61, n=1108	85.43 ± 29.40, n=410	0.19457
Substance					
Sitagliptin	44.6 % (1101/2469)	45.3 % (431/951)	42.3 % (469/1108)	49.0 % (201/410)	0.05608
Vildagliptin	47.3 % (1169/2469)	47.0 % (447/951)	48.6 % (539/1108)	44.6 % (183/410)	0.36683
Linagliptin	0.0 % (0/2469)	0.0 % (0/951)	0.0 % (0/1108)	0.0 % (0/410)	
Saxagliptin	7.5 % (186/2469)	7.3 % (69/951)	8.8 % (97/1108)	4.9 % (20/410)	0.03638
Other	0.5 % (13/2469)	0.4 % (4/951)	0.3 % (3/1108)	1.5 % (6/410)	0.01456
GLP-1 analogs/mimetics	5.1 % (211/4130)	4.0 % (67/1671)	6.1 % (110/1808)	5.2 % (34/651)	0.02097
GLP-1 analogs/mimetics, dosage [mg/day]	7.73 ± 15.46, n=211	5.92 ± 9.39, n=67	8.92 ± 17.67, n=110	7.48 ± 17.34, n=34	0.86890
Substance					
Exenatide	41.7 % (88/211)	32.8 % (22/67)	46.4 % (51/110)	44.1 % (15/34)	0.19878
Liraglutide	57.3 % (121/211)	65.7 % (44/67)	52.7 % (58/110)	55.9 % (19/34)	0.23601
Other	0.9 % (2/211)	1.5 % (1/67)	0.9 % (1/110)	0.0 % (0/34)	0.76383
SGTL-2 inhibitors	2.9 % (120/4130)	2.7 % (45/1671)	2.7 % (48/1808)	4.1 % (27/651)	0.12067
SGTL-2 inhibitors, dosage [mg/day]	14.55 ± 19.87, n=119	14.22 ± 18.86, n=45	15.66 ± 22.27, n=47	13.15 ± 17.55, n=27	0.52403
Substance					
Dapagliflozin	89.2 % (107/120)	84.4 % (38/45)	93.8 % (45/48)	88.9 % (24/27)	0.35260
Other	10.8 % (13/120)	15.6 % (7/45)	6.3 % (3/48)	11.1 % (3/27)	0.35260
Insulin(rapid-acting or long-acting or Pre-mixed)	20.0 % (824/4130)	13.6 % (227/1671)	22.3 % (404/1808)	29.6 % (193/651)	<.00001
Rapid-acting insulin	7.6 % (314/4130)	5.6 % (93/1671)	7.5 % (135/1808)	13.2 % (86/651)	<.00001
Human insulin	40.8 % (128/314)	48.4 % (45/93)	36.3 % (49/135)	39.5 % (34/86)	0.18197
Analogues	59.2 % (186/314)	51.6 % (48/93)	63.7 % (86/135)	60.5 % (52/86)	0.18197
Syringe	2.9 % (9/314)	1.1 % (1/93)	2.2 % (3/135)	5.8 % (5/86)	0.13830
Pen	97.1 % (305/314)	98.9 % (92/93)	97.8 % (132/135)	94.2 % (81/86)	0.13830

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
Pump	0.0 % (0/314)	0.0 % (0/93)	0.0 % (0/135)	0.0 % (0/86)	
Other	0.0 % (0/314)	0.0 % (0/93)	0.0 % (0/135)	0.0 % (0/86)	
U-40	15.7 % (49/312)	16.1 % (15/93)	15.8 % (21/133)	15.1 % (13/86)	0.98223
U-100	84.3 % (263/312)	83.9 % (78/93)	84.2 % (112/133)	84.9 % (73/86)	0.98223
1x insulin/day	8.9 % (28/314)	8.6 % (8/93)	5.2 % (7/135)	15.1 % (13/86)	0.04086
2x insulin/day	13.1 % (41/314)	15.1 % (14/93)	14.1 % (19/135)	9.3 % (8/86)	0.46823
3x insulin/day	76.1 % (239/314)	75.3 % (70/93)	78.5 % (106/135)	73.3 % (63/86)	0.65302
4x insulin/day	1.9 % (6/314)	1.1 % (1/93)	2.2 % (3/135)	2.3 % (2/86)	0.78068
Long-acting insulin	18.5 % (763/4130)	12.4 % (208/1671)	21.0 % (379/1808)	27.0 % (176/651)	<.00001
Human insulin	30.7 % (234/763)	31.7 % (66/208)	29.8 % (113/379)	31.3 % (55/176)	0.87453
Analogues	69.3 % (529/763)	68.3 % (142/208)	70.2 % (266/379)	68.8 % (121/176)	0.87453
Syringe	4.8 % (37/763)	6.3 % (13/208)	4.7 % (18/379)	3.4 % (6/176)	0.43089
Pen	94.6 % (722/763)	93.3 % (194/208)	94.5 % (358/379)	96.6 % (170/176)	0.34817
Pump	0.1 % (1/763)	0.0 % (0/208)	0.3 % (1/379)	0.0 % (0/176)	0.60214
Other	0.4 % (3/763)	0.5 % (1/208)	0.5 % (2/379)	0.0 % (0/176)	0.63426
U-40	13.3 % (101/761)	15.4 % (32/208)	10.1 % (38/377)	17.6 % (31/176)	0.02980
U-100	86.7 % (660/761)	84.6 % (176/208)	89.9 % (339/377)	82.4 % (145/176)	0.02980
1x insulin/day	87.0 % (664/763)	85.1 % (177/208)	87.3 % (331/379)	88.6 % (156/176)	0.57055
2x insulin/day	12.2 % (93/763)	13.0 % (27/208)	12.1 % (46/379)	11.4 % (20/176)	0.88923
3x insulin/day	0.7 % (5/763)	1.4 % (3/208)	0.5 % (2/379)	0.0 % (0/176)	0.19843
4x insulin/day	0.1 % (1/763)	0.5 % (1/208)	0.0 % (0/379)	0.0 % (0/176)	0.26293
Pre-mixed insulin	2.3 % (96/4130)	1.0 % (16/1671)	2.9 % (52/1808)	4.3 % (28/651)	<.00001
Human insulin	69.8 % (67/96)	81.3 % (13/16)	73.1 % (38/52)	57.1 % (16/28)	0.18383
Analogues	30.2 % (29/96)	18.8 % (3/16)	26.9 % (14/52)	42.9 % (12/28)	0.18383
Syringe	3.1 % (3/96)	0.0 % (0/16)	3.8 % (2/52)	3.6 % (1/28)	0.73202
Pen	96.9 % (93/96)	100.0 % (16/16)	96.2 % (50/52)	96.4 % (27/28)	0.73202
Pump	0.0 % (0/96)	0.0 % (0/16)	0.0 % (0/52)	0.0 % (0/28)	

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
Other	0.0 % (0/96)	0.0 % (0/16)	0.0 % (0/52)	0.0 % (0/28)	
U-40	12.8 % (12/94)	25.0 % (4/16)	7.8 % (4/51)	14.8 % (4/27)	0.18619
U-100	87.2 % (82/94)	75.0 % (12/16)	92.2 % (47/51)	85.2 % (23/27)	0.18619
1x insulin/day	10.4 % (10/96)	6.3 % (1/16)	9.6 % (5/52)	14.3 % (4/28)	0.67617
2x insulin/day	79.2 % (76/96)	81.3 % (13/16)	80.8 % (42/52)	75.0 % (21/28)	0.81147
3x insulin/day	9.4 % (9/96)	12.5 % (2/16)	7.7 % (4/52)	10.7 % (3/28)	0.81208
4x insulin/day	1.0 % (1/96)	0.0 % (0/16)	1.9 % (1/52)	0.0 % (0/28)	0.65212
Fixed-dose combination metformin / DPP-4 inhibitor	77.5 % (1563/2016)	77.5 % (579/747)	76.6 % (702/917)	80.1 % (282/352)	0.39646
Novartis drugs					
Vildagliptin / Metformin					
Eucreas	92.5 % (727/786)	93.1 % (255/274)	93.0 % (345/371)	90.1 % (127/141)	0.48340
Icandra	7.5 % (59/786)	6.9 % (19/274)	7.0 % (26/371)	9.9 % (14/141)	0.48340
Vildagliptin					
Galvus	87.7 % (335/382)	87.3 % (151/173)	89.8 % (150/167)	81.0 % (34/42)	0.28708
Jalra	12.3 % (47/382)	12.7 % (22/173)	10.2 % (17/167)	19.0 % (8/42)	0.28708
Nateglinide					
STARLIX	100.0 % (4/4)	100.0 % (1/1)	100.0 % (2/2)	100.0 % (1/1)	
Other	0.0 % (0/4)	0.0 % (0/1)	0.0 % (0/2)	0.0 % (0/1)	

Table 9-56. *Anti-hypertensive therapy in the HbA1c treatment groups at 24-month follow-up.*

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
No. of patients with FU data	4130 (100.0 %)	1671 (40.5 %)	1808 (43.8 %)	651 (15.8 %)	
ACE inhibitors	52.8 % (2179/4130)	51.4 % (859/1671)	53.4 % (966/1808)	54.4 % (354/651)	0.32676
ACE inhibitors, dosage [mg/day]	10.0 (5.0, 10.0)	7.5 (5.0, 10.0)	10.0 (5.0, 10.0)	10.0 (5.0, 10.0)	0.52195
Substance					
Captopril	2.5 % (54/2179)	2.7 % (23/859)	2.5 % (24/966)	2.0 % (7/354)	0.77540
Enalapril	19.9 % (434/2179)	22.0 % (189/859)	17.7 % (171/966)	20.9 % (74/354)	0.06298
Lisinopril	10.6 % (230/2179)	9.9 % (85/859)	11.7 % (113/966)	9.0 % (32/354)	0.27345
Ramipril	64.1 % (1397/2179)	62.5 % (537/859)	65.6 % (634/966)	63.8 % (226/354)	0.38036
Trandolapril	0.2 % (4/2179)	0.2 % (2/859)	0.1 % (1/966)	0.3 % (1/354)	0.72593
Other	2.8 % (60/2179)	2.7 % (23/859)	2.4 % (23/966)	4.0 % (14/354)	0.29715
Angiotensin receptor blocker (ARB)	29.9 % (1235/4130)	29.0 % (484/1671)	31.4 % (568/1808)	28.1 % (183/651)	0.15930
ARB, dosage [mg/day]	80.0 (20.0, 160.0)	80.0 (32.0, 160.0)	80.0 (20.0, 160.0)	80.0 (20.0, 160.0)	0.56714
Substance					
Candesartan	24.0 % (296/1235)	23.6 % (114/484)	23.6 % (134/568)	26.2 % (48/183)	0.73958
Irbesartan	5.1 % (63/1235)	6.0 % (29/484)	4.8 % (27/568)	3.8 % (7/183)	0.46064
Losartan	7.2 % (89/1235)	7.6 % (37/484)	6.7 % (38/568)	7.7 % (14/183)	0.81087
Valsartan	40.2 % (497/1235)	39.5 % (191/484)	41.0 % (233/568)	39.9 % (73/183)	0.87155
Other	23.5 % (290/1235)	23.3 % (113/484)	23.9 % (136/568)	22.4 % (41/183)	0.90912
Direct renin inhibitor	0.3 % (12/4130)	0.5 % (8/1671)	0.2 % (4/1808)	0.0 % (0/651)	0.12005
Direct renin inhibitor, dosage [mg/day]	225.0 (150.0, 300.0)	150.0 (150.0, 300.0)	300.0 (225.0, 300.0)		0.25684[U]
Beta-blocker	49.7 % (2053/4130)	48.6 % (812/1671)	51.1 % (924/1808)	48.7 % (317/651)	0.28487
Beta-blocker, dosage [mg/day]	25.0 (5.0, 95.0)	25.0 (5.0, 95.0)	47.5 (5.0, 100.0)	10.0 (5.0, 95.0)	0.00714
Substance					
Metoprolol	45.9 % (942/2053)	46.4 % (377/812)	47.9 % (443/924)	38.5 % (122/317)	0.01315

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
Bisoprolol	41.1 % (844/2053)	41.0 % (333/812)	39.1 % (361/924)	47.3 % (150/317)	0.03615
Nebivolol	5.6 % (115/2053)	6.2 % (50/812)	4.5 % (42/924)	7.3 % (23/317)	0.13109
Carvedilol	4.1 % (85/2053)	3.6 % (29/812)	4.5 % (42/924)	4.4 % (14/317)	0.57547
Other	3.3 % (67/2053)	2.8 % (23/812)	3.9 % (36/924)	2.5 % (8/317)	0.33310
Calcium channel blocker	30.6 % (1264/4130)	28.8 % (481/1671)	31.2 % (564/1808)	33.6 % (219/651)	0.05709
Calcium channel blocker, dosage [mg/day]	10.0 (5.0, 10.0)	10.0 (5.0, 10.0)	10.0 (5.0, 10.0)	10.0 (5.0, 10.0)	0.39339
Substance					
Amlodipine	76.0 % (961/1264)	74.2 % (357/481)	77.8 % (439/564)	75.3 % (165/219)	0.38072
Nifedipine	1.8 % (23/1264)	1.7 % (8/481)	2.0 % (11/564)	1.8 % (4/219)	0.94182
Nisoldipine	0.0 % (0/1264)	0.0 % (0/481)	0.0 % (0/564)	0.0 % (0/219)	
Nimodipine	0.1 % (1/1264)	0.2 % (1/481)	0.0 % (0/564)	0.0 % (0/219)	0.44283
Diltiazem	0.7 % (9/1264)	0.4 % (2/481)	0.4 % (2/564)	2.3 % (5/219)	0.00974
Verapamil	2.6 % (33/1264)	2.5 % (12/481)	2.3 % (13/564)	3.7 % (8/219)	0.55754
Gallopamil	0.0 % (0/1264)	0.0 % (0/481)	0.0 % (0/564)	0.0 % (0/219)	
Felodipine	2.8 % (36/1264)	2.5 % (12/481)	3.2 % (18/564)	2.7 % (6/219)	0.79191
Nitrendipine	4.4 % (55/1264)	4.8 % (23/481)	4.8 % (27/564)	2.3 % (5/219)	0.25635
Lercanidipine	10.2 % (129/1264)	12.5 % (60/481)	7.8 % (44/564)	11.4 % (25/219)	0.03674
Nilvadipine	0.1 % (1/1264)	0.0 % (0/481)	0.2 % (1/564)	0.0 % (0/219)	0.53738
Manidipine	0.1 % (1/1264)	0.2 % (1/481)	0.0 % (0/564)	0.0 % (0/219)	0.44283
Isradipine	0.1 % (1/1264)	0.2 % (1/481)	0.0 % (0/564)	0.0 % (0/219)	0.44283
Other	1.1 % (14/1264)	0.8 % (4/481)	1.6 % (9/564)	0.5 % (1/219)	0.29988
Diuretic drugs	45.3 % (1871/4130)	43.5 % (727/1671)	46.0 % (831/1808)	48.1 % (313/651)	0.10443
Diuretic drugs, dosage [mg/day]	20.0 (12.5, 25.0)	20.0 (12.5, 25.0)	20.0 (12.5, 25.0)	12.5 (12.5, 25.0)	0.25469
Substance					
Furosemide	7.6 % (143/1871)	6.6 % (48/727)	9.4 % (78/831)	5.4 % (17/313)	0.03236
Torasemide	21.9 % (409/1871)	20.5 % (149/727)	21.5 % (179/831)	25.9 % (81/313)	0.14944
Bumetanide	0.1 % (1/1871)	0.0 % (0/727)	0.1 % (1/831)	0.0 % (0/313)	0.53468

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
Etacrynic acid	0.1 % (1/1871)	0.0 % (0/727)	0.1 % (1/831)	0.0 % (0/313)	0.53468
Piretanide	1.4 % (27/1871)	2.1 % (15/727)	1.2 % (10/831)	0.6 % (2/313)	0.15530
Hydrochlorothiazide	71.5 % (1337/1871)	75.1 % (546/727)	69.8 % (580/831)	67.4 % (211/313)	0.01519
Clopamid	0.3 % (5/1871)	0.3 % (2/727)	0.4 % (3/831)	0.0 % (0/313)	0.57277
Other	8.3 % (156/1871)	6.1 % (44/727)	8.9 % (74/831)	12.1 % (38/313)	0.00362
Other anti-hypertensive therapy	11.1 % (457/4130)	9.2 % (154/1671)	12.5 % (226/1808)	11.8 % (77/651)	0.00683
Fixed-dose combinations					
Fixed-dose combination ARB/calcium channel blocker/diuretic	72.7 % (277/381)	71.8 % (102/142)	73.6 % (131/178)	72.1 % (44/61)	0.93430
Fixed-dose combination ACE inhibitor/diuretic	50.4 % (469/931)	53.8 % (200/372)	47.6 % (190/399)	49.4 % (79/160)	0.22483
Fixed-dose combination ARB/diuretic	65.3 % (328/502)	67.0 % (130/194)	67.0 % (150/224)	57.1 % (48/84)	0.22401
Fixed-dose combination ARB/calcium channel blocker	41.3 % (114/276)	43.0 % (46/107)	44.5 % (57/128)	26.8 % (11/41)	0.12132
Fixed-dose combination ACE inhibitor/calcium channel blocker	16.9 % (104/614)	19.1 % (44/230)	15.4 % (40/260)	16.1 % (20/124)	0.52482
Fixed-dose combination direct renin inhibitor/diuretic	44.4 % (4/9)	50.0 % (3/6)	33.3 % (1/3)		0.63526
Novartis drugs					
Valsartan / Hydrochlorothiazide					
CoDiovan	27.0 % (31/115)	34.1 % (15/44)	24.6 % (14/57)	14.3 % (2/14)	0.29449
Codiovan forte	11.3 % (13/115)	18.2 % (8/44)	8.8 % (5/57)	0.0 % (0/14)	0.12096
Cordinate plus	3.5 % (4/115)	4.5 % (2/44)	1.8 % (1/57)	7.1 % (1/14)	0.54503
Provas	0.9 % (1/115)	0.0 % (0/44)	1.8 % (1/57)	0.0 % (0/14)	0.59856
Provas comp	4.3 % (5/115)	4.5 % (2/44)	5.3 % (3/57)	0.0 % (0/14)	0.68546
Provas maxx	1.7 % (2/115)	2.3 % (1/44)	1.8 % (1/57)	0.0 % (0/14)	0.85164
Other	51.3 % (59/115)	36.4 % (16/44)	56.1 % (32/57)	78.6 % (11/14)	0.01336
Valsartan					
Cordinate	2.0 % (3/151)	3.2 % (2/62)	0.0 % (0/64)	4.0 % (1/25)	0.31561
Diovan	27.8 % (42/151)	32.3 % (20/62)	25.0 % (16/64)	24.0 % (6/25)	0.59351
Provas	7.3 % (11/151)	6.5 % (4/62)	7.8 % (5/64)	8.0 % (2/25)	0.94694
Other	62.9 % (95/151)	58.1 % (36/62)	67.2 % (43/64)	64.0 % (16/25)	0.56595

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
Valsartan / Amlodipine / Hydrochlorothiazide					
Exforge HCT	73.6 % (103/140)	78.8 % (41/52)	69.7 % (46/66)	72.7 % (16/22)	0.53214
Dafiro HCT	15.7 % (22/140)	13.5 % (7/52)	16.7 % (11/66)	18.2 % (4/22)	0.84132
Other	10.7 % (15/140)	7.7 % (4/52)	13.6 % (9/66)	9.1 % (2/22)	0.56380
Aliskiren					
Rasilez	100.0 % (8/8)	100.0 % (5/5)	100.0 % (3/3)		
Other	0.0 % (0/8)	0.0 % (0/5)	0.0 % (0/3)		
Hydrochlorothiazide					
Esidrix	4.6 % (16/346)	4.1 % (6/148)	6.3 % (9/143)	1.8 % (1/55)	0.36886
Other	95.4 % (330/346)	95.9 % (142/148)	93.7 % (134/143)	98.2 % (54/55)	0.36886
Aliskiren / Hydrochlorothiazide					
Rasilez HCT	75.0 % (3/4)	66.7 % (2/3)	100.0 % (1/1)		0.50499
Other	25.0 % (1/4)	33.3 % (1/3)	0.0 % (0/1)		0.50499
Valsartan / Amlodipine					
Exforge	80.8 % (59/73)	75.0 % (21/28)	81.1 % (30/37)	100.0 % (8/8)	0.28476
Dafiro	13.7 % (10/73)	17.9 % (5/28)	13.5 % (5/37)	0.0 % (0/8)	0.43160
Other	5.5 % (4/73)	7.1 % (2/28)	5.4 % (2/37)	0.0 % (0/8)	0.73574

Table 9-57. *Hypoglycemic events in the HbA1c treatment groups at 24-month follow-up.*

	TOTAL	HbA1c <= 6.5	HbA1c >6.5 - <=7	HbA1c >7 - <=7.5	P-value
No. of patients with FU data	4130 (100.0 %)	1671 (40.5 %)	1808 (43.8 %)	651 (15.8 %)	
Hypoglycemic events since last FU					
Without specific symptoms	0.3 % (12/4039)	0.2 % (4/1650)	0.3 % (6/1753)	0.3 % (2/636)	0.86341
No. of events	1.92 ± 1.44, n=12	1.75 ± 0.96, n=4	2.33 ± 1.86, n=6	1.00 ± 0.00, n=2	0.34835
Symptomatic, but controllable without external help	0.2 % (10/4073)	0.1 % (1/1654)	0.4 % (7/1775)	0.3 % (2/644)	0.13334
No. of events	4.20 ± 3.82, n=10	3.00, n=1	3.57 ± 3.21, n=7	7.00 ± 7.07, n=2	0.69376
External help needed	0.0 % (0/4079)	0.0 % (0/1655)	0.0 % (0/1780)	0.0 % (0/644)	
No. of events	, n=0	, n=0	, n=0	, n=0	
Symptomatic with medical help	0.0 % (0/4079)	0.0 % (0/1655)	0.0 % (0/1780)	0.0 % (0/644)	
No. of events	, n=0	, n=0	, n=0	, n=0	
Hospitalization required	0.0 % (1/4079)	0.0 % (0/1655)	0.1 % (1/1780)	0.0 % (0/644)	0.52417
No. of events	1.00, n=1	, n=0	1.00, n=1	, n=0	

9.4.2 Treatment success in the SBP treatment target groups

9.4.2.1 SBP target achievement

Table 9-58 shows frequency distributions of SBP target achievement rates at 6, 12, and 24 months follow-up.

Table 9-58. *Frequency distributions of SBP target achievement rates at 6-, 12-, and 24-month follow-up.*

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
No. of patients with 6M-FU data	7327 (100.0 %)	2836 (38.7 %)	2518 (34.4 %)	1973 (26.9 %)	
Target SBP met	56.1 % (4097/7303)	51.4 % (1453/2827)	54.5 % (1370/2516)	65.0 % (1274/1960)	<.00001
No. of patients with 12M-FU data	6666 (100.0 %)	2632 (39.5 %)	2311 (34.7 %)	1723 (25.8 %)	
Target SBP met	57.0 % (3786/6643)	50.8 % (1334/2625)	56.4 % (1298/2303)	67.3 % (1154/1715)	<.00001
No. of patients with 24-M FU data	4116 (100.0 %)	1636 (39.7 %)	1427 (34.7 %)	1053 (25.6 %)	
Target SBP met	59.5 % (2438/4097)	50.3 % (818/1627)	60.6 % (860/1420)	72.4 % (760/1050)	<.00001

9.4.2.2 Patient characteristics

Patient characteristics at 6-month follow-up

Table 9-59 shows vital status and cause of death in the SBP treatment groups at 6-month follow-up.

Table 9-60 shows newly diagnosed diseases and other events in the SBP treatment groups at 6-month follow-up.

Table 9-61 shows absolute and relative changes in clinical parameters (i.e. SBP; DBP, Heart rate; Weight; BMI; Waist circumference) in the SBP treatment groups at 6-month follow-up.

Table 9-62 shows absolute and relative changes in laboratory values (i.e. Cholesterol; Glucose; Haemoglobin; Creatinine; Liver function) in the SBP treatment groups at 6-month follow-up.

Table 9-59. *Vital status and cause of death in the SBP treatment groups at 6-month follow-up.*

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
No. of patients with FU data	7327 (100.0 %)	2836 (38.7 %)	2518 (34.4 %)	1973 (26.9 %)	
FU date missing	0.1 % (4/7327)	0.1 % (3/2836)	0.0 % (1/2518)	0.0 % (0/1973)	0.28057
Vital status missing	0.1 % (5/7327)	0.1 % (3/2836)	0.0 % (0/2518)	0.1 % (2/1973)	0.26940
No. of days until 6-month FU	184.0 (177.0, 196.0)	184.0 (177.0, 196.0)	184.0 (177.0, 196.0)	185.0 (177.0, 198.0)	0.51862
Mortality	0.2 % (13/7322)	0.2 % (5/2833)	0.2 % (5/2518)	0.2 % (3/1971)	0.93502
Sudden cardiac death	15.4 % (2/13)	20.0 % (1/5)	0.0 % (0/5)	33.3 % (1/3)	0.42035
Other cardiovascular causes	7.7 % (1/13)	20.0 % (1/5)	0.0 % (0/5)	0.0 % (0/3)	0.42035
Cancer	38.5 % (5/13)	40.0 % (2/5)	40.0 % (2/5)	33.3 % (1/3)	0.97857
Other	23.1 % (3/13)	20.0 % (1/5)	40.0 % (2/5)	0.0 % (0/3)	0.42035
Unknown	15.4 % (2/13)	0.0 % (0/5)	20.0 % (1/5)	33.3 % (1/3)	0.42035
No. of days until death	134.0 (86.5, 156.5)	131.0 (99.0, 153.0)	144.0 (104.0, 160.5)	82.0 (8.0, 246.0)	0.80830

Table 9-60. *Newly diagnosed diseases and other events in the SBP treatment groups at 6-month follow-up.*

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
No. of patients with FU data	7327 (100.0 %)	2836 (38.7 %)	2518 (34.4 %)	1973 (26.9 %)	
Coronary Heart Disease	0.2 % (18/7287)	0.4 % (10/2816)	0.1 % (2/2508)	0.3 % (6/1963)	0.10768
Myocardial infarction	0.1 % (10/7287)	0.1 % (3/2816)	0.0 % (1/2508)	0.3 % (6/1963)	0.05000
PCI	0.2 % (17/7286)	0.2 % (7/2816)	0.1 % (2/2507)	0.4 % (8/1963)	0.07704
CABG	0.0 % (1/7287)	0.0 % (0/2816)	0.0 % (0/2508)	0.1 % (1/1963)	0.25762
Peripheral angioplasty	0.1 % (6/7287)	0.1 % (3/2816)	0.1 % (3/2508)	0.0 % (0/1963)	0.32601
Peripheral bypass surgery	0.0 % (2/7286)	0.0 % (0/2816)	0.0 % (1/2508)	0.1 % (1/1962)	0.51952
Stroke/TIA	0.2 % (16/7286)	0.2 % (5/2815)	0.3 % (7/2508)	0.2 % (4/1963)	0.72102
Heart Failure	0.3 % (21/7285)	0.1 % (2/2814)	0.3 % (8/2508)	0.6 % (11/1963)	0.00761
NYHA I	23.8 % (5/21)	50.0 % (1/2)	25.0 % (2/8)	18.2 % (2/11)	0.62047
NYHA II	33.3 % (7/21)	0.0 % (0/2)	25.0 % (2/8)	45.5 % (5/11)	0.37208
NYHA III	33.3 % (7/21)	50.0 % (1/2)	25.0 % (2/8)	36.4 % (4/11)	0.76130
NYHA IV	9.5 % (2/21)	0.0 % (0/2)	25.0 % (2/8)	0.0 % (0/11)	0.16595
Peripheral arterial occlusive disease	0.2 % (14/7286)	0.2 % (5/2815)	0.2 % (6/2508)	0.2 % (3/1963)	0.78695
Dyslipidemia	0.3 % (22/7285)	0.2 % (5/2815)	0.4 % (10/2508)	0.4 % (7/1962)	0.29800
Autonomous neuropathy	0.1 % (10/7285)	0.1 % (4/2814)	0.1 % (3/2508)	0.2 % (3/1963)	0.95287
Non-proliferative diabetic retinopathy	0.1 % (4/7301)	0.0 % (1/2830)	0.0 % (0/2508)	0.2 % (3/1963)	0.08142
Proliferative diabetic retinopathy / laser coagulation	0.0 % (2/7300)	0.0 % (1/2830)	0.0 % (0/2508)	0.1 % (1/1962)	0.56259
Diabetic macular edema	0.0 % (1/7300)	0.0 % (0/2830)	0.0 % (0/2507)	0.1 % (1/1963)	0.25677
Blindness	0.0 % (1/7300)	0.0 % (0/2829)	0.0 % (0/2508)	0.1 % (1/1963)	0.25677
Dialysis	0.0 % (2/7301)	0.0 % (1/2831)	0.0 % (1/2507)	0.0 % (0/1963)	0.68873
Amputation	0.1 % (4/7327)	0.0 % (1/2836)	0.1 % (2/2518)	0.1 % (1/1973)	0.78489
Foot	25.0 % (1/4)	100.0 % (1/1)	0.0 % (0/2)	0.0 % (0/1)	0.13534
Toes	75.0 % (3/4)	0.0 % (0/1)	100.0 % (2/2)	100.0 % (1/1)	0.13534
Upper extremities	0.0 % (0/4)	0.0 % (0/1)	0.0 % (0/2)	0.0 % (0/1)	
Lower extremities	0.0 % (0/4)	0.0 % (0/1)	0.0 % (0/2)	0.0 % (0/1)	
Rehospitalisation	3.2 % (232/7300)	2.7 % (76/2819)	2.9 % (73/2516)	4.2 % (83/1965)	0.00767
Reasons					

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
Cardiac	21.6 % (50/232)	19.7 % (15/76)	17.8 % (13/73)	26.5 % (22/83)	0.37566
Diabetes	4.7 % (11/232)	2.6 % (2/76)	6.8 % (5/73)	4.8 % (4/83)	0.47991
Other	73.7 % (171/232)	78.9 % (60/76)	76.7 % (56/73)	66.3 % (55/83)	0.15039
Unknown	1.3 % (3/232)	1.3 % (1/76)	0.0 % (0/73)	2.4 % (2/83)	0.41327
Duration [weeks]	1.0 (1.0, 2.0)	1.0 (1.0, 2.0)	1.0 (1.0, 2.0)	1.0 (1.0, 2.0)	0.92891
Rehabilitation measures	0.8 % (55/7282)	0.9 % (24/2816)	0.5 % (13/2515)	0.9 % (18/1951)	0.22439
Reasons					
Cardiac	9.1 % (5/55)	8.3 % (2/24)	0.0 % (0/13)	16.7 % (3/18)	0.27711
Diabetes	21.8 % (12/55)	33.3 % (8/24)	15.4 % (2/13)	11.1 % (2/18)	0.18352
Other	69.1 % (38/55)	62.5 % (15/24)	84.6 % (11/13)	66.7 % (12/18)	0.36699
Unknown	1.8 % (1/55)	0.0 % (0/24)	0.0 % (0/13)	5.6 % (1/18)	0.35106
As out-patient	36.4 % (20/55)	33.3 % (8/24)	30.8 % (4/13)	44.4 % (8/18)	0.67740
As in-patient	63.6 % (35/55)	66.7 % (16/24)	69.2 % (9/13)	55.6 % (10/18)	0.67740
Duration [weeks]	3.0 (3.0, 4.0)	3.0 (3.0, 3.0)	3.0 (3.0, 5.0)	3.0 (3.0, 3.0)	0.51543
General practitioner consultations	89.6 % (6542/7298)	87.6 % (2468/2816)	91.9 % (2312/2516)	89.6 % (1762/1966)	<.00001
No. of contacts	5.01 ± 4.35, n=6542	5.31 ± 4.72, n=2468	4.59 ± 3.84, n=2312	5.12 ± 4.39, n=1762	<.00001
Specialist physician consultations	54.2 % (3957/7297)	50.6 % (1423/2815)	58.1 % (1463/2516)	54.5 % (1071/1966)	<.00001
No. of contacts	2.28 ± 2.23, n=3957	2.25 ± 1.89, n=1423	2.27 ± 2.28, n=1463	2.35 ± 2.55, n=1071	0.21339

Table 9-61. *Absolute and relative changes in clinical parameters in the SBP treatment groups at 6-month follow-up.*

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
No. of patients with FU data	7327 (100.0 %)	2836 (38.7 %)	2518 (34.4 %)	1973 (26.9 %)	
Systolic blood pressure	135.82 ± 13.88, n=7304	133.57 ± 13.40, n=2828	135.85 ± 13.27, n=2516	139.02 ± 14.69, n=1960	<.00001
Absolute change [FU - BL]	-4.57 ± 15.99, n=7295	-3.05 ± 16.37, n=2828	-5.17 ± 15.22, n=2508	-6.00 ± 16.23, n=1959	<.00001
Relative change [(FU - BL)/BL]	-0.03 ± 0.11, n=7295	-0.01 ± 0.12, n=2828	-0.03 ± 0.10, n=2508	-0.04 ± 0.11, n=1959	<.00001
[SBP FU6 - target SBP]	1.41 ± 13.84, n=7303	3.57 ± 13.40, n=2827	0.85 ± 13.27, n=2516	-0.98 ± 14.69, n=1960	<.00001
Target SBP met	56.1 % (4097/7303)	51.4 % (1453/2827)	54.5 % (1370/2516)	65.0 % (1274/1960)	<.00001
Diastolic blood pressure	80.56 ± 8.55, n=7304	80.07 ± 8.27, n=2828	80.57 ± 8.28, n=2516	81.26 ± 9.21, n=1960	0.00002
Absolute change [FU - BL]	-2.16 ± 9.91, n=7295	-1.31 ± 10.08, n=2828	-2.46 ± 9.34, n=2508	-2.99 ± 10.27, n=1959	<.00001
Relative change [(FU - BL)/BL]	-0.02 ± 0.13, n=7295	-0.01 ± 0.13, n=2828	-0.02 ± 0.11, n=2508	-0.03 ± 0.13, n=1959	<.00001
[DBP FU6 - target SBP]	-3.02 ± 8.92, n=7304	-0.35 ± 8.32, n=2828	-3.65 ± 8.35, n=2516	-6.06 ± 9.35, n=1960	<.00001
Target DBP met	76.0 % (5553/7303)	68.8 % (1946/2827)	77.3 % (1945/2516)	84.8 % (1662/1960)	<.00001
Heart rate [/min]	74.09 ± 9.35, n=7284	73.86 ± 9.41, n=2814	74.04 ± 9.01, n=2514	74.46 ± 9.68, n=1956	0.12930
Absolute change [FU - BL]	-0.98 ± 9.72, n=7268	-0.79 ± 10.02, n=2809	-1.13 ± 9.69, n=2505	-1.05 ± 9.33, n=1954	0.07594
Relative change [(FU - BL)/BL]	-0.00 ± 0.13, n=7268	-0.00 ± 0.14, n=2809	-0.01 ± 0.13, n=2505	-0.01 ± 0.12, n=1954	0.10227
Weight [kg]	89.74 ± 18.40, n=7308	89.51 ± 18.51, n=2831	89.82 ± 17.91, n=2516	89.99 ± 18.88, n=1961	0.65495
Absolute change [FU - BL]	-0.68 ± 5.02, n=7306	-0.71 ± 5.65, n=2831	-0.70 ± 4.60, n=2515	-0.61 ± 4.53, n=1960	0.11390
Relative change [(FU - BL)/BL]	-0.01 ± 0.06, n=7306	-0.01 ± 0.06, n=2831	-0.01 ± 0.05, n=2515	-0.01 ± 0.05, n=1960	0.09123
BMI [kg/m2]	31.03 ± 5.85, n=7301	30.90 ± 5.84, n=2830	31.00 ± 5.65, n=2511	31.27 ± 6.09, n=1960	0.23527
Absolute change [FU - BL]	-0.23 ± 1.77, n=7301	-0.24 ± 1.98, n=2830	-0.23 ± 1.61, n=2511	-0.20 ± 1.63, n=1960	0.11879
Relative change [(FU - BL)/BL]	-0.01 ± 0.06, n=7301	-0.01 ± 0.06, n=2830	-0.01 ± 0.05, n=2511	-0.01 ± 0.05, n=1960	0.10081
BMI < 25	11.2 % (816/7301)	11.7 % (332/2830)	10.5 % (264/2511)	11.2 % (220/1960)	0.36908
BMI: 25 - 30	38.4 % (2806/7301)	38.7 % (1096/2830)	39.1 % (981/2511)	37.2 % (729/1960)	0.40578

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
BMI > 30	50.4 % (3679/7301)	49.5 % (1402/2830)	50.4 % (1266/2511)	51.6 % (1011/1960)	0.38082
Waist circumference [cm]	108.79 ± 18.03, n=2223	108.73 ± 16.94, n=865	108.76 ± 18.83, n=888	108.97 ± 18.47, n=470	0.30642
Absolute change [FU - BL]	0.03 ± 10.29, n=1985	-0.88 ± 7.87, n=781	0.80 ± 12.59, n=804	0.27 ± 9.12, n=400	0.48259
Relative change [(FU - BL)/BL]	0.00 ± 0.10, n=1985	-0.01 ± 0.07, n=781	0.01 ± 0.12, n=804	0.00 ± 0.09, n=400	0.59057
Diabetes training since baseline	24.7 % (1801/7295)	24.8 % (702/2829)	26.6 % (670/2515)	22.0 % (429/1951)	0.00164
Participation in DMP diabetes	83.7 % (6106/7295)	84.3 % (2386/2829)	83.0 % (2088/2515)	83.6 % (1632/1951)	0.42681

Table 9-62. *Absolute and relative changes in the laboratory values in the SBP treatment groups at 6-month follow-up.*

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
No. of patients with FU data	7327 (100.0 %)	2836 (38.7 %)	2518 (34.4 %)	1973 (26.9 %)	
Total fasting cholesterol available	68.0 % (4981/7327)	64.7 % (1835/2836)	72.1 % (1815/2518)	67.5 % (1331/1973)	<.00001
Total fasting cholesterol [mmol/L]	9.79 ± 3.21, n=4981	9.77 ± 3.15, n=1835	9.84 ± 3.13, n=1815	9.73 ± 3.38, n=1331	0.61727
Absolute change [FU - BL]	4.45 ± 2.88, n=4657	4.53 ± 2.81, n=1703	4.53 ± 2.77, n=1722	4.25 ± 3.09, n=1232	0.07595
Relative change [(FU - BL)/BL]	0.87 ± 0.55, n=4657	0.89 ± 0.55, n=1703	0.88 ± 0.53, n=1722	0.81 ± 0.57, n=1232	0.00063
Fasting HDL-cholesterol available	56.4 % (4132/7327)	54.3 % (1541/2836)	60.9 % (1533/2518)	53.6 % (1058/1973)	<.00001
Fasting HDL-cholesterol [mmol/L]	1.27 ± 0.37, n=4132	1.29 ± 0.38, n=1541	1.26 ± 0.36, n=1533	1.27 ± 0.37, n=1058	0.31955
Absolute change [FU - BL]	0.01 ± 0.29, n=3716	0.02 ± 0.30, n=1382	0.01 ± 0.30, n=1390	0.01 ± 0.28, n=944	0.71769
Relative change [(FU - BL)/BL]	0.05 ± 0.80, n=3716	0.04 ± 0.30, n=1382	0.06 ± 1.27, n=1390	0.02 ± 0.17, n=944	0.67285
Fasting LDL-cholesterol available	55.8 % (4092/7327)	53.2 % (1509/2836)	60.0 % (1512/2518)	54.3 % (1071/1973)	<.00001
Fasting LDL-cholesterol [mmol/L]	3.09 ± 0.95, n=4092	3.01 ± 0.93, n=1509	3.09 ± 0.93, n=1512	3.20 ± 1.01, n=1071	<.00001
Absolute change [FU - BL]	-0.12 ± 0.76, n=3678	-0.11 ± 0.77, n=1365	-0.12 ± 0.74, n=1364	-0.14 ± 0.78, n=949	0.32894
Relative change [(FU - BL)/BL]	0.06 ± 1.67, n=3678	0.03 ± 0.93, n=1365	0.13 ± 2.48, n=1364	0.02 ± 0.88, n=949	0.35753
Fasting triglycerides available	59.6 % (4370/7327)	57.8 % (1638/2836)	64.5 % (1624/2518)	56.2 % (1108/1973)	<.00001
Fasting triglycerides [mmol/L]	2.11 ± 1.29, n=4370	2.10 ± 1.25, n=1638	2.09 ± 1.28, n=1624	2.15 ± 1.37, n=1108	0.51311
Absolute change [FU - BL]	-0.19 ± 1.16, n=3977	-0.16 ± 1.25, n=1489	-0.16 ± 1.06, n=1485	-0.25 ± 1.15, n=1003	0.03464
Relative change [(FU - BL)/BL]	0.05 ± 1.51, n=3977	0.06 ± 0.78, n=1489	0.00 ± 0.50, n=1485	0.10 ± 2.79, n=1003	0.05789
Fasting glucose available	72.8 % (5333/7327)	69.6 % (1975/2836)	76.3 % (1920/2518)	72.9 % (1438/1973)	<.00001
Fasting glucose [mmol/L]	7.42 ± 2.15, n=5333	7.23 ± 2.12, n=1975	7.41 ± 2.06, n=1920	7.70 ± 2.29, n=1438	<.00001
Absolute change [FU - BL]	-1.04 ± 2.68, n=5057	-0.88 ± 2.57, n=1874	-1.23 ± 2.72, n=1831	-1.03 ± 2.75, n=1352	<.00001
Relative change [(FU - BL)/BL]	-0.07 ± 0.44, n=5057	-0.06 ± 0.29, n=1874	-0.08 ± 0.62, n=1831	-0.07 ± 0.28, n=1352	0.00001
Postprandial glucose available	39.3 % (2877/7327)	37.6 % (1065/2836)	41.8 % (1053/2518)	38.5 % (759/1973)	0.00430

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
Postprandial glucose [mmol/L]	8.88 ± 2.77, n=2877	8.85 ± 2.67, n=1065	8.87 ± 2.44, n=1053	8.94 ± 3.30, n=759	0.02478
Absolute change [FU - BL]	-1.87 ± 3.29, n=2415	-1.52 ± 3.24, n=901	-2.26 ± 3.17, n=919	-1.81 ± 3.51, n=595	<.00001
Relative change [(FU - BL)/BL]	-0.07 ± 1.09, n=2415	-0.07 ± 0.82, n=901	-0.07 ± 1.50, n=919	-0.09 ± 0.57, n=595	<.00001
HbA1c [%]	7.11 ± 1.04, n=6698	6.98 ± 1.05, n=2547	7.15 ± 0.98, n=2350	7.23 ± 1.07, n=1801	<.00001
[HbA1c FU6 - target HbA1c]	0.22 ± 0.99, n=6698	0.30 ± 1.02, n=2547	0.20 ± 0.94, n=2350	0.12 ± 1.01, n=1801	<.00001
Target HbA1c met	49.5 % (3315/6698)	45.9 % (1169/2547)	49.5 % (1163/2350)	54.6 % (983/1801)	<.00001
Absolute change [FU - BL]	-0.66 ± 1.27, n=6500	-0.55 ± 1.27, n=2466	-0.76 ± 1.25, n=2292	-0.70 ± 1.30, n=1742	<.00001
Relative change [(FU - BL)/BL]	-0.07 ± 0.13, n=6500	-0.06 ± 0.13, n=2466	-0.08 ± 0.13, n=2292	-0.07 ± 0.13, n=1742	<.00001
Haemoglobin available	48.2 % (3529/7327)	45.5 % (1289/2836)	53.1 % (1337/2518)	45.8 % (903/1973)	<.00001
Haemoglobin [mmol/L]	8.36 ± 1.35, n=3529	8.32 ± 1.32, n=1289	8.40 ± 1.39, n=1337	8.36 ± 1.31, n=903	0.02631
Absolute change [FU - BL]	-0.01 ± 0.69, n=3060	0.04 ± 0.81, n=1113	-0.01 ± 0.57, n=1177	-0.06 ± 0.67, n=770	0.11882
Relative change [(FU - BL)/BL]	0.00 ± 0.11, n=3060	0.01 ± 0.13, n=1113	0.00 ± 0.10, n=1177	-0.00 ± 0.09, n=770	0.12490
Serum creatinine available	72.2 % (5291/7327)	72.1 % (2045/2836)	74.8 % (1884/2518)	69.0 % (1362/1973)	0.00010
Serum creatinine [µmol/l]	83.70 ± 37.85, n=5291	83.25 ± 48.84, n=2045	82.99 ± 29.45, n=1884	85.36 ± 27.99, n=1362	0.00019
Absolute change [FU - BL]	-1.64 ± 58.56, n=4837	-3.11 ± 81.70, n=1863	-0.77 ± 38.96, n=1738	-0.67 ± 35.00, n=1236	0.05669
Relative change [(FU - BL)/BL]	0.02 ± 0.36, n=4837	0.02 ± 0.53, n=1863	0.01 ± 0.20, n=1738	0.02 ± 0.18, n=1236	0.04571
Microalbustix albumin [mg/l]	19.84 ± 33.59, n=1612	21.19 ± 31.81, n=558	20.57 ± 35.25, n=651	16.79 ± 33.15, n=403	<.00001
Microalbustix creatinine [mg/dl]	38.10 ± 73.39, n=907	52.74 ± 82.77, n=311	34.30 ± 70.84, n=324	25.89 ± 61.46, n=272	<.00001
Macroalbuminuria: positive test	6.8 % (264/3894)	6.1 % (89/1461)	6.4 % (89/1397)	8.3 % (86/1036)	0.07214
Macroalbuminuria: negative test	93.2 % (3630/3894)	93.9 % (1372/1461)	93.6 % (1308/1397)	91.7 % (950/1036)	0.07214
Increased liver function readings	12.1 % (513/4231)	13.0 % (209/1605)	9.9 % (151/1527)	13.9 % (153/1099)	0.00287

Patient characteristics at 12-month follow-up

Table 9-63 shows vital status and cause of death in the SBP treatment groups at 12-month follow-up.

Table 9-64 shows newly diagnosed diseases and other events in the SBP treatment groups at 12-month follow-up.

Table 9-65 shows absolute and relative changes in clinical parameters (i.e. SBP; DBP, Heart rate; Weight; BMI; Waist circumference) in the SBP treatment groups at 12-month follow-up.

Table 9-66 shows absolute and relative changes in laboratory values (i.e. Cholesterol; Glucose; Haemoglobin; Creatinine; Liver function) in the SBP treatment groups at 12-month follow-up.

Table 9-63. *Vital status and cause of death in the SBP treatment groups at 12-month follow-up.*

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
No. of patients with FU data	6666 (100.0 %)	2632 (39.5 %)	2311 (34.7 %)	1723 (25.8 %)	
FU date missing	0.1 % (5/6666)	0.0 % (1/2632)	0.1 % (2/2311)	0.1 % (2/1723)	0.63449
Vital status missing	0.1 % (7/6666)	0.2 % (4/2632)	0.1 % (2/2311)	0.1 % (1/1723)	0.60928
No. of days until 12-month FU	367.0 (361.0, 380.0)	368.0 (360.0, 379.0)	367.0 (360.0, 379.0)	368.0 (361.0, 383.0)	0.09426
Cumulative 1-years-Mortality	0.3 % (23/8536)	0.2 % (8/3319)	0.3 % (9/2853)	0.3 % (6/2364)	0.84115
Sudden cardiac death	17.4 % (4/23)	12.5 % (1/8)	11.1 % (1/9)	33.3 % (2/6)	0.48634
Other cardiovascular causes	13.0 % (3/23)	12.5 % (1/8)	0.0 % (0/9)	33.3 % (2/6)	0.17120
Cancer	26.1 % (6/23)	25.0 % (2/8)	33.3 % (3/9)	16.7 % (1/6)	0.76869
Other	26.1 % (6/23)	25.0 % (2/8)	44.4 % (4/9)	0.0 % (0/6)	0.15759
Unknown	17.4 % (4/23)	25.0 % (2/8)	11.1 % (1/9)	16.7 % (1/6)	0.75140
No. of days until death	193.0 (131.0, 254.0)	156.5 (115.0, 280.0)	197.5 (144.0, 266.5)	224.0 (82.0, 246.0)	0.87213

Table 9-64. *Newly diagnosed diseases and other events in the SBP treatment groups at 12-month follow-up.*

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
No. of patients with FU data	6666 (100.0 %)	2632 (39.5 %)	2311 (34.7 %)	1723 (25.8 %)	
Coronary Heart Disease	0.3 % (18/6650)	0.3 % (7/2629)	0.4 % (9/2304)	0.1 % (2/1717)	0.25383
Myocardial infarction	0.1 % (9/6650)	0.1 % (2/2629)	0.2 % (5/2304)	0.1 % (2/1717)	0.39346
PCI	0.1 % (8/6650)	0.1 % (2/2629)	0.2 % (4/2304)	0.1 % (2/1717)	0.61416
CABG	0.2 % (10/6650)	0.1 % (2/2629)	0.3 % (6/2304)	0.1 % (2/1717)	0.22808
Peripheral angioplasty	0.1 % (5/6649)	0.1 % (3/2629)	0.0 % (1/2304)	0.1 % (1/1716)	0.63598
Peripheral bypass surgery	0.0 % (1/6650)	0.0 % (1/2629)	0.0 % (0/2304)	0.0 % (0/1717)	0.46540
Stroke/TIA	0.2 % (10/6650)	0.1 % (2/2629)	0.2 % (5/2304)	0.2 % (3/1717)	0.42405
Heart Failure	0.3 % (18/6651)	0.2 % (5/2629)	0.2 % (5/2305)	0.5 % (8/1717)	0.19175
NYHA I	11.1 % (2/18)	0.0 % (0/5)	20.0 % (1/5)	12.5 % (1/8)	0.59433
NYHA II	16.7 % (3/18)	20.0 % (1/5)	0.0 % (0/5)	25.0 % (2/8)	0.48675
NYHA III	61.1 % (11/18)	60.0 % (3/5)	80.0 % (4/5)	50.0 % (4/8)	0.55743
NYHA IV	11.1 % (2/18)	20.0 % (1/5)	0.0 % (0/5)	12.5 % (1/8)	0.59433
Peripheral arterial occlusive disease	0.2 % (14/6649)	0.1 % (3/2628)	0.3 % (7/2304)	0.2 % (4/1717)	0.34008
Dyslipidemia	0.2 % (13/6650)	0.1 % (2/2629)	0.2 % (4/2304)	0.4 % (7/1717)	0.05129
Autonomous neuropathy	0.1 % (6/6649)	0.1 % (2/2628)	0.1 % (2/2304)	0.1 % (2/1717)	0.90828
Non-proliferative diabetic retinopathy	0.0 % (0/6649)	0.0 % (0/2628)	0.0 % (0/2304)	0.0 % (0/1717)	
Proliferative diabetic retinopathy / laser coagulation	0.0 % (2/6649)	0.0 % (1/2628)	0.0 % (0/2304)	0.1 % (1/1717)	0.54837
Diabetic macular edema	0.0 % (2/6649)	0.0 % (0/2628)	0.0 % (1/2304)	0.1 % (1/1717)	0.50168
Blindness	0.0 % (0/6649)	0.0 % (0/2628)	0.0 % (0/2304)	0.0 % (0/1717)	
Dialysis	0.0 % (2/6649)	0.0 % (0/2628)	0.0 % (1/2304)	0.1 % (1/1717)	0.50168
Amputation	0.0 % (0/6666)	0.0 % (0/2632)	0.0 % (0/2311)	0.0 % (0/1723)	
Foot					
Toes					
Upper extremities					
Lower extremities					
Rehospitalisation	2.5 % (167/6652)	2.2 % (59/2629)	2.4 % (56/2306)	3.0 % (52/1717)	0.25823
Reasons					
Cardiac	35.3 % (59/167)	37.3 % (22/59)	35.7 % (20/56)	32.7 % (17/52)	0.87767
Diabetes	3.0 % (5/167)	3.4 % (2/59)	1.8 % (1/56)	3.8 % (2/52)	0.80118
Other	62.9 % (105/167)	61.0 % (36/59)	62.5 % (35/56)	65.4 % (34/52)	0.89095
Unknown	0.6 % (1/167)	1.7 % (1/59)	0.0 % (0/56)	0.0 % (0/52)	0.39821

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
Duration [weeks]	1.0 (1.0, 2.0)	1.0 (1.0, 2.0)	1.0 (1.0, 2.0)	1.0 (1.0, 2.0)	0.84764
Rehabilitation measures	0.7 % (46/6650)	0.7 % (18/2630)	0.7 % (16/2304)	0.7 % (12/1716)	0.99814
Reasons					
Cardiac	37.0 % (17/46)	33.3 % (6/18)	50.0 % (8/16)	25.0 % (3/12)	0.36676
Diabetes	6.5 % (3/46)	11.1 % (2/18)	6.3 % (1/16)	0.0 % (0/12)	0.48166
Other	56.5 % (26/46)	61.1 % (11/18)	43.8 % (7/16)	66.7 % (8/12)	0.42340
Unknown	2.2 % (1/46)	0.0 % (0/18)	0.0 % (0/16)	8.3 % (1/12)	0.23501
As out-patient	10.9 % (5/46)	11.1 % (2/18)	0.0 % (0/16)	25.0 % (3/12)	0.10940
As in-patient	89.1 % (41/46)	88.9 % (16/18)	100.0 % (16/16)	75.0 % (9/12)	0.10940
Duration [weeks]	3.0 (3.0, 4.0)	3.0 (3.0, 4.0)	3.0 (3.0, 3.5)	3.0 (3.0, 3.5)	0.88030
General practitioner consultations	90.5 % (6016/6651)	89.0 % (2341/2630)	90.6 % (2089/2305)	92.4 % (1586/1716)	0.00085
No. of contacts	4.0 (2.0, 6.0)	4.0 (2.0, 6.0)	3.0 (2.0, 6.0)	4.0 (2.0, 6.0)	0.01928
Specialist physician consultations	56.3 % (3742/6651)	51.1 % (1344/2630)	60.7 % (1399/2305)	58.2 % (999/1716)	<.00001
No. of contacts	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)	2.0 (1.0, 2.0)	2.0 (1.0, 3.0)	0.00273

Table 9-65. *Absolute and relative changes in clinical parameters in the SBP treatment groups at 12-month follow-up.*

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
No. of patients with FU data	6666 (100.0 %)	2632 (39.5 %)	2311 (34.7 %)	1723 (25.8 %)	
Systolic blood pressure	135.36 ± 13.48, n=6644	133.55 ± 13.06, n=2626	135.24 ± 12.98, n=2303	138.27 ± 14.25, n=1715	<.00001
Absolute change [FU - BL]	-4.88 ± 16.48, n=6638	-3.33 ± 16.88, n=2626	-5.67 ± 15.90, n=2298	-6.22 ± 16.44, n=1714	<.00001
Relative change [(FU - BL)/BL]	-0.03 ± 0.11, n=6638	-0.02 ± 0.12, n=2626	-0.03 ± 0.11, n=2298	-0.04 ± 0.11, n=1714	<.00001
[SBP FU12 - target SBP]	1.04 ± 13.52, n=6643	3.55 ± 13.06, n=2625	0.24 ± 12.98, n=2303	-1.73 ± 14.25, n=1715	<.00001
Target SBP met	57.0 % (3786/6643)	50.8 % (1334/2625)	56.4 % (1298/2303)	67.3 % (1154/1715)	<.00001
Diastolic blood pressure	80.34 ± 8.12, n=6644	79.71 ± 8.05, n=2626	80.37 ± 7.79, n=2303	81.27 ± 8.58, n=1715	<.00001
Absolute change [FU - BL]	-2.45 ± 10.04, n=6638	-1.82 ± 10.23, n=2626	-2.76 ± 9.56, n=2298	-2.99 ± 10.32, n=1714	0.00003
Relative change [(FU - BL)/BL]	-0.02 ± 0.13, n=6638	-0.01 ± 0.13, n=2626	-0.03 ± 0.12, n=2298	-0.03 ± 0.13, n=1714	0.00010
[DBP FU12 - target SBP]	-3.18 ± 8.56, n=6644	-0.70 ± 8.10, n=2626	-3.84 ± 7.97, n=2303	-6.10 ± 8.92, n=1715	<.00001
Target DBP met	77.0 % (5116/6643)	70.6 % (1852/2625)	78.7 % (1813/2303)	84.6 % (1451/1715)	<.00001
Heart rate [/min]	73.82 ± 9.00, n=6626	73.76 ± 8.84, n=2611	73.66 ± 8.87, n=2302	74.15 ± 9.41, n=1713	0.29616
Absolute change [FU - BL]	-1.30 ± 10.55, n=6611	-1.07 ± 10.50, n=2605	-1.60 ± 10.33, n=2295	-1.24 ± 10.90, n=1711	0.01873
Relative change [(FU - BL)/BL]	-0.01 ± 0.14, n=6611	-0.00 ± 0.14, n=2605	-0.01 ± 0.14, n=2295	-0.01 ± 0.15, n=1711	0.01545
Weight [kg]	89.39 ± 18.21, n=6644	89.12 ± 18.10, n=2626	89.50 ± 17.99, n=2303	89.65 ± 18.67, n=1715	0.74022
Absolute change [FU - BL]	-0.97 ± 5.63, n=6643	-1.00 ± 6.03, n=2626	-1.04 ± 5.59, n=2303	-0.82 ± 5.02, n=1714	0.09036
Relative change [(FU - BL)/BL]	-0.01 ± 0.06, n=6643	-0.01 ± 0.07, n=2626	-0.01 ± 0.06, n=2303	-0.01 ± 0.05, n=1714	0.07254
BMI [kg/m2]	30.92 ± 5.75, n=6640	30.78 ± 5.72, n=2626	30.93 ± 5.67, n=2300	31.10 ± 5.90, n=1714	0.21992
Absolute change [FU - BL]	-0.33 ± 1.95, n=6640	-0.34 ± 2.10, n=2626	-0.35 ± 1.92, n=2300	-0.28 ± 1.73, n=1714	0.11031
Relative change [(FU - BL)/BL]	-0.01 ± 0.06, n=6640	-0.01 ± 0.07, n=2626	-0.01 ± 0.06, n=2300	-0.01 ± 0.05, n=1714	0.07637
BMI < 25	11.8 % (785/6640)	11.9 % (313/2626)	11.3 % (261/2300)	12.3 % (211/1714)	0.63379
BMI: 25 - 30	38.0 % (2521/6640)	39.1 % (1028/2626)	38.9 % (895/2300)	34.9 % (598/1714)	0.00946

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
BMI > 30	50.2 % (3334/6640)	48.9 % (1285/2626)	49.7 % (1144/2300)	52.8 % (905/1714)	0.03847
Waist circumference [cm]	107.04 ± 15.26, n=1839	108.08 ± 15.59, n=739	105.89 ± 14.10, n=750	107.31 ± 16.77, n=350	0.00757
Absolute change [FU - BL]	-1.10 ± 7.61, n=1625	-1.49 ± 7.48, n=659	-1.12 ± 7.21, n=675	-0.15 ± 8.69, n=291	0.10501
Relative change [(FU - BL)/BL]	-0.01 ± 0.07, n=1625	-0.01 ± 0.07, n=659	-0.01 ± 0.08, n=675	-0.00 ± 0.08, n=291	0.08472
Diabetes training FU12	32.6 % (2166/6646)	34.7 % (912/2626)	32.3 % (744/2304)	29.7 % (510/1716)	0.00248
Participation in DMP diabetes	83.2 % (5527/6646)	84.8 % (2227/2626)	82.6 % (1902/2304)	81.5 % (1398/1716)	0.01008

Table 9-66. *Absolute and relative changes in laboratory values in the SBP treatment groups at 12-month follow-up.*

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
No. of patients with FU data	6666 (100.0 %)	2632 (39.5 %)	2311 (34.7 %)	1723 (25.8 %)	
Total fasting cholesterol available	67.0 % (4463/6666)	61.5 % (1618/2632)	73.6 % (1702/2311)	66.3 % (1143/1723)	<.00001
Total fasting cholesterol [mmol/L]	9.68 ± 3.23, n=4463	9.66 ± 3.14, n=1618	9.81 ± 3.16, n=1702	9.52 ± 3.44, n=1143	0.17082
Absolute change [FU - BL]	4.34 ± 2.95, n=4223	4.44 ± 2.79, n=1531	4.46 ± 2.85, n=1615	4.00 ± 3.28, n=1077	0.01365
Relative change [(FU - BL)/BL]	0.85 ± 0.57, n=4223	0.89 ± 0.56, n=1531	0.87 ± 0.56, n=1615	0.77 ± 0.61, n=1077	<.00001
Fasting HDL-cholesterol available	53.9 % (3596/6666)	50.2 % (1321/2632)	59.4 % (1373/2311)	52.4 % (902/1723)	<.00001
Fasting HDL-cholesterol [mmol/L]	1.28 ± 0.37, n=3596	1.30 ± 0.38, n=1321	1.27 ± 0.35, n=1373	1.28 ± 0.37, n=902	0.33902
Absolute change [FU - BL]	0.03 ± 0.32, n=3293	0.04 ± 0.32, n=1213	0.03 ± 0.31, n=1265	0.01 ± 0.33, n=815	0.06686
Relative change [(FU - BL)/BL]	0.05 ± 0.31, n=3293	0.06 ± 0.32, n=1213	0.05 ± 0.27, n=1265	0.04 ± 0.34, n=815	0.06622
Fasting LDL-cholesterol available	53.6 % (3573/6666)	49.4 % (1301/2632)	58.8 % (1360/2311)	52.9 % (912/1723)	<.00001
Fasting LDL-cholesterol [mmol/L]	3.06 ± 0.97, n=3573	2.95 ± 0.94, n=1301	3.08 ± 0.95, n=1360	3.17 ± 1.02, n=912	<.00001
Absolute change [FU - BL]	-0.16 ± 0.83, n=3259	-0.15 ± 0.80, n=1192	-0.13 ± 0.83, n=1247	-0.20 ± 0.88, n=820	0.18442
Relative change [(FU - BL)/BL]	0.10 ± 2.24, n=3259	0.01 ± 0.88, n=1192	0.13 ± 2.67, n=1247	0.19 ± 2.83, n=820	0.16954
Fasting triglycerides available	58.9 % (3923/6666)	54.6 % (1437/2632)	66.6 % (1540/2311)	54.9 % (946/1723)	<.00001
Fasting triglycerides [mmol/L]	2.11 ± 1.36, n=3923	2.09 ± 1.28, n=1437	2.11 ± 1.49, n=1540	2.14 ± 1.25, n=946	0.27515
Absolute change [FU - BL]	-0.20 ± 1.30, n=3607	-0.19 ± 1.39, n=1325	-0.16 ± 1.28, n=1424	-0.28 ± 1.19, n=858	0.02962
Relative change [(FU - BL)/BL]	0.04 ± 1.38, n=3607	0.04 ± 0.64, n=1325	-0.00 ± 0.50, n=1424	0.09 ± 2.63, n=858	0.04126
Fasting glucose available	70.6 % (4705/6666)	67.4 % (1773/2632)	75.0 % (1734/2311)	69.5 % (1198/1723)	<.00001
Fasting glucose [mmol/L]	7.38 ± 2.16, n=4705	7.19 ± 2.04, n=1773	7.39 ± 2.17, n=1734	7.64 ± 2.28, n=1198	<.00001
Absolute change [FU - BL]	-1.13 ± 2.84, n=4463	-0.94 ± 2.81, n=1688	-1.30 ± 2.83, n=1656	-1.15 ± 2.89, n=1119	<.00001
Relative change [(FU - BL)/BL]	-0.07 ± 0.63, n=4463	-0.05 ± 0.64, n=1688	-0.09 ± 0.53, n=1656	-0.07 ± 0.73, n=1119	<.00001
Postprandial glucose available	40.0 % (2669/6666)	37.4 % (985/2632)	44.6 % (1031/2311)	37.9 % (653/1723)	<.00001

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
Postprandial glucose [mmol/L]	8.76 ± 4.33, n=2669	8.75 ± 6.02, n=985	8.72 ± 2.58, n=1031	8.83 ± 3.41, n=653	0.00213
Absolute change [FU - BL]	-2.17 ± 4.99, n=2213	-1.71 ± 6.96, n=797	-2.58 ± 3.25, n=904	-2.17 ± 3.61, n=512	<.00001
Relative change [(FU - BL)/BL]	-0.11 ± 1.06, n=2213	-0.07 ± 1.08, n=797	-0.13 ± 1.30, n=904	-0.15 ± 0.28, n=512	0.00001
HbA1c [%]	7.05 ± 1.00, n=6052	6.93 ± 1.00, n=2340	7.09 ± 0.98, n=2152	7.18 ± 1.00, n=1560	<.00001
[HbA1c FU12 - target HbA1c]	0.16 ± 0.97, n=6052	0.25 ± 0.98, n=2340	0.14 ± 0.95, n=2152	0.07 ± 0.96, n=1560	<.00001
Target HbA1c met	53.0 % (3210/6052)	47.9 % (1122/2340)	54.8 % (1179/2152)	58.3 % (909/1560)	<.00001
Absolute change [FU - BL]	-0.73 ± 1.29, n=5873	-0.61 ± 1.29, n=2264	-0.83 ± 1.25, n=2103	-0.78 ± 1.32, n=1506	<.00001
Relative change [(FU - BL)/BL]	-0.08 ± 0.13, n=5873	-0.07 ± 0.14, n=2264	-0.09 ± 0.13, n=2103	-0.08 ± 0.13, n=1506	<.00001
Haemoglobin available	47.5 % (3165/6666)	42.5 % (1118/2632)	56.3 % (1300/2311)	43.4 % (747/1723)	<.00001
Haemoglobin [mmol/L]	8.35 ± 1.34, n=3165	8.35 ± 1.29, n=1118	8.35 ± 1.37, n=1300	8.35 ± 1.35, n=747	0.66883
Absolute change [FU - BL]	0.00 ± 0.77, n=2748	0.03 ± 0.83, n=991	0.01 ± 0.80, n=1115	-0.05 ± 0.63, n=642	0.71820
Relative change [(FU - BL)/BL]	0.01 ± 0.15, n=2748	0.01 ± 0.15, n=991	0.01 ± 0.19, n=1115	-0.00 ± 0.08, n=642	0.73042
Serum creatinine available	72.1 % (4804/6666)	71.3 % (1876/2632)	76.9 % (1778/2311)	66.7 % (1150/1723)	<.00001
Serum creatinine [µmol/l]	84.73 ± 49.14, n=4804	85.02 ± 63.17, n=1876	83.20 ± 40.23, n=1778	86.62 ± 32.75, n=1150	0.00049
Absolute change [FU - BL]	-0.04 ± 57.99, n=4419	-0.62 ± 77.21, n=1723	0.26 ± 41.78, n=1640	0.43 ± 40.48, n=1056	0.01581
Relative change [(FU - BL)/BL]	0.03 ± 0.49, n=4419	0.04 ± 0.66, n=1723	0.02 ± 0.40, n=1640	0.04 ± 0.22, n=1056	0.01994
Microalbustix albumin [mg/l]	19.72 ± 33.61, n=1479	22.43 ± 33.64, n=494	19.10 ± 33.00, n=649	16.94 ± 34.53, n=336	<.00001
Microalbustix creatinine [mg/dl]	43.54 ± 78.69, n=829	50.83 ± 79.87, n=279	46.41 ± 81.76, n=319	30.78 ± 71.43, n=231	<.00001
Macroalbuminuria: positive test	7.0 % (246/3523)	6.0 % (77/1290)	7.7 % (104/1343)	7.3 % (65/890)	0.18454
Macroalbuminuria: negative test	93.0 % (3277/3523)	94.0 % (1213/1290)	92.3 % (1239/1343)	92.7 % (825/890)	0.18454
Increased liver function readings	10.3 % (400/3889)	10.3 % (154/1491)	9.3 % (136/1464)	11.8 % (110/934)	0.14741

Patient characteristics at 24-month follow-up

Table 9-67 shows vital status and cause of death in the SBP treatment groups at 24-month follow-up.

Table 9-68 shows newly diagnosed diseases and other events in the SBP treatment groups at 24-month follow-up.

Table 9-69 shows absolute and relative changes in clinical parameters (i.e. SBP; DBP, Heart rate; Weight; BMI; Waist circumference) in the SBP treatment groups at 24-month follow-up.

Table 9-70 shows absolute and relative changes in laboratory values (i.e. Cholesterol; Glucose; Haemoglobin; Creatinine; Liver function) in the SBP treatment groups at 24-month follow-up.

Table 9-67. *Vital status and cause of death in the SBP treatment groups at 24-month follow-up.*

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
No. of patients with FU data	4116 (100.0 %)	1636 (39.7 %)	1427 (34.7 %)	1053 (25.6 %)	
FU date missing	0.1 % (6/4116)	0.2 % (3/1636)	0.1 % (2/1427)	0.1 % (1/1053)	0.83999
Vital status missing	0.1 % (4/4116)	0.1 % (2/1636)	0.1 % (2/1427)	0.0 % (0/1053)	0.49618
No. of days until 24-month FU	726.0 (696.0, 736.0)	727.0 (705.0, 738.0)	721.0 (678.0, 734.0)	729.0 (700.0, 739.0)	<.00001
Cumulative 2-year Mortality	0.4 % (35/8536)	0.4 % (14/3319)	0.4 % (12/2853)	0.4 % (9/2364)	0.96615
Sudden cardiac death	14.3 % (5/35)	14.3 % (2/14)	8.3 % (1/12)	22.2 % (2/9)	0.66692
Other cardiovascular causes	14.3 % (5/35)	7.1 % (1/14)	0.0 % (0/12)	44.4 % (4/9)	0.00971
Cancer	34.3 % (12/35)	42.9 % (6/14)	33.3 % (4/12)	22.2 % (2/9)	0.59373
Other	25.7 % (9/35)	21.4 % (3/14)	50.0 % (6/12)	0.0 % (0/9)	0.03088
Unknown	11.4 % (4/35)	14.3 % (2/14)	8.3 % (1/12)	11.1 % (1/9)	0.89254
No. of days until death	259.5 (153.0, 471.0)	339.0 (153.0, 496.0)	265.0 (151.0, 406.0)	246.0 (223.0, 488.0)	0.83968

Table 9-68. *Newly diagnosed diseases and other events in the SBP treatment groups at 24-month follow-up.*

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
No. of patients with FU data	4116 (100.0 %)	1636 (39.7 %)	1427 (34.7 %)	1053 (25.6 %)	
Coronary Heart Disease	0.3 % (11/4102)	0.4 % (7/1629)	0.2 % (3/1423)	0.1 % (1/1050)	0.23009
Myocardial infarction	0.2 % (8/4101)	0.1 % (2/1629)	0.3 % (4/1423)	0.2 % (2/1049)	0.61285
PCI	0.3 % (14/4101)	0.4 % (6/1629)	0.4 % (6/1423)	0.2 % (2/1049)	0.60512
CABG	0.0 % (1/4101)	0.1 % (1/1629)	0.0 % (0/1423)	0.0 % (0/1049)	0.46817
Peripheral angioplasty	0.0 % (2/4101)	0.1 % (1/1629)	0.0 % (0/1423)	0.1 % (1/1049)	0.54497
Peripheral bypass surgery	0.0 % (1/4101)	0.1 % (1/1629)	0.0 % (0/1423)	0.0 % (0/1049)	0.46817
Stroke/TIA	0.3 % (11/4101)	0.3 % (5/1629)	0.2 % (3/1423)	0.3 % (3/1049)	0.86983
Heart Failure	0.2 % (10/4101)	0.2 % (3/1629)	0.1 % (2/1423)	0.5 % (5/1049)	0.20190
NYHA I	10.0 % (1/10)	0.0 % (0/3)	0.0 % (0/2)	20.0 % (1/5)	0.57375
NYHA II	50.0 % (5/10)	100.0 % (3/3)	50.0 % (1/2)	20.0 % (1/5)	0.09072
NYHA III	40.0 % (4/10)	0.0 % (0/3)	50.0 % (1/2)	60.0 % (3/5)	0.23262
NYHA IV	0.0 % (0/10)	0.0 % (0/3)	0.0 % (0/2)	0.0 % (0/5)	
Peripheral arterial occlusive disease	0.1 % (4/4101)	0.2 % (3/1629)	0.0 % (0/1423)	0.1 % (1/1049)	0.26656
Dyslipidemia	0.1 % (5/4101)	0.1 % (1/1629)	0.1 % (2/1423)	0.2 % (2/1049)	0.62571
Autonomous neuropathy	0.2 % (8/4100)	0.1 % (2/1628)	0.0 % (0/1423)	0.6 % (6/1049)	0.00436
Non-proliferative diabetic retinopathy	0.0 % (1/4100)	0.1 % (1/1628)	0.0 % (0/1423)	0.0 % (0/1049)	0.46795
Proliferative diabetic retinopathy / laser coagulation	0.0 % (0/4100)	0.0 % (0/1628)	0.0 % (0/1423)	0.0 % (0/1049)	
Diabetic macular edema	0.0 % (0/4100)	0.0 % (0/1628)	0.0 % (0/1423)	0.0 % (0/1049)	
Blindness	0.0 % (0/4100)	0.0 % (0/1628)	0.0 % (0/1423)	0.0 % (0/1049)	
Dialysis	0.0 % (2/4100)	0.1 % (1/1628)	0.1 % (1/1423)	0.0 % (0/1049)	0.70463
Amputation	0.0 % (0/4116)	0.0 % (0/1636)	0.0 % (0/1427)	0.0 % (0/1053)	
Foot					
Toes					

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
Upper extremities					
Lower extremities					
Rehospitalisation	3.2 % (131/4100)	3.3 % (54/1627)	2.6 % (37/1422)	3.8 % (40/1051)	0.22698
Reasons					
Cardiac	30.5 % (40/131)	35.2 % (19/54)	29.7 % (11/37)	25.0 % (10/40)	0.56564
Diabetes	4.6 % (6/131)	3.7 % (2/54)	8.1 % (3/37)	2.5 % (1/40)	0.46193
Other	64.9 % (85/131)	59.3 % (32/54)	64.9 % (24/37)	72.5 % (29/40)	0.41310
Unknown	2.3 % (3/131)	3.7 % (2/54)	0.0 % (0/37)	2.5 % (1/40)	0.50730
Duration [weeks]	1.0 (1.0, 2.0)	1.0 (1.0, 2.0)	1.0 (1.0, 2.0)	2.0 (1.0, 2.0)	0.80529
Rehabilitation measures	1.2 % (50/4102)	1.3 % (21/1628)	0.7 % (10/1423)	1.8 % (19/1051)	0.04407
Reasons					
Cardiac	24.0 % (12/50)	38.1 % (8/21)	10.0 % (1/10)	15.8 % (3/19)	0.13106
Diabetes	4.0 % (2/50)	0.0 % (0/21)	10.0 % (1/10)	5.3 % (1/19)	0.38840
Other	70.0 % (35/50)	61.9 % (13/21)	90.0 % (9/10)	68.4 % (13/19)	0.27491
Unknown	4.0 % (2/50)	0.0 % (0/21)	0.0 % (0/10)	10.5 % (2/19)	0.18276
As out-patient	12.0 % (6/50)	0.0 % (0/21)	20.0 % (2/10)	21.1 % (4/19)	0.08441
As in-patient	88.0 % (44/50)	100.0 % (21/21)	80.0 % (8/10)	78.9 % (15/19)	0.08441
Duration [weeks]	3.0 (3.0, 4.0)	3.0 (3.0, 3.0)	4.0 (3.0, 4.0)	3.0 (3.0, 4.0)	0.11385
General practitioner consultations	92.8 % (3807/4102)	92.9 % (1513/1628)	93.1 % (1325/1423)	92.2 % (969/1051)	0.66210
No. of contacts	5.0 (3.0, 10.0)	6.0 (3.0, 10.0)	5.0 (4.0, 8.0)	6.0 (3.0, 10.0)	0.01263
Specialist physician consultations	62.4 % (2561/4102)	58.7 % (955/1628)	66.4 % (945/1423)	62.9 % (661/1051)	0.00006
No. of contacts	2.0 (1.0, 4.0)	2.0 (1.0, 4.0)	2.0 (1.0, 4.0)	2.0 (1.0, 4.0)	0.00329

Table 9-69. *Absolute and relative changes in clinical parameters in the SBP treatment groups at 24-month follow-up.*

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
No. of patients with FU data	4116 (100.0 %)	1636 (39.7 %)	1427 (34.7 %)	1053 (25.6 %)	
Systolic blood pressure	134.94 ± 12.86, n=4097	133.96 ± 12.22, n=1627	134.50 ± 13.06, n=1420	137.05 ± 13.29, n=1050	<.00001
Absolute change (FU24-Basis)	-5.51 ± 16.83, n=4097	-3.09 ± 16.75, n=1627	-6.50 ± 16.71, n=1420	-7.91 ± 16.65, n=1050	<.00001
Relative change (FU24-Basis/Basis)	-0.03 ± 0.12, n=4097	-0.01 ± 0.12, n=1627	-0.04 ± 0.12, n=1420	-0.05 ± 0.11, n=1050	<.00001
[SBP FU24 - target SBP]	0.64 ± 13.11, n=4097	3.96 ± 12.22, n=1627	-0.50 ± 13.06, n=1420	-2.95 ± 13.29, n=1050	<.00001
Target SBP met	59.5 % (2438/4097)	50.3 % (818/1627)	60.6 % (860/1420)	72.4 % (760/1050)	<.00001
Diastolic blood pressure	80.60 ± 7.95, n=4097	80.43 ± 7.78, n=1627	80.49 ± 7.82, n=1420	81.00 ± 8.38, n=1050	0.22605
Absolute change [FU - BL]	-2.46 ± 10.39, n=4097	-1.51 ± 10.30, n=1627	-2.70 ± 10.00, n=1420	-3.63 ± 10.89, n=1050	<.00001
Relative change [(FU - BL)/BL]	-0.02 ± 0.13, n=4097	-0.01 ± 0.13, n=1627	-0.02 ± 0.12, n=1420	-0.03 ± 0.15, n=1050	<.00001
[SBP FU24 - target SBP]	0.64 ± 13.11, n=4097	3.96 ± 12.22, n=1627	-0.50 ± 13.06, n=1420	-2.95 ± 13.29, n=1050	<.00001
Target DBP met	76.1 % (3119/4097)	67.0 % (1090/1627)	79.7 % (1132/1420)	85.4 % (897/1050)	<.00001
Heart rate [/min]	74.01 ± 8.62, n=4094	74.13 ± 8.83, n=1624	74.02 ± 8.44, n=1420	73.81 ± 8.54, n=1050	0.54470
Absolute change [FU - BL]	-1.00 ± 10.67, n=4085	-0.33 ± 10.78, n=1618	-1.42 ± 10.53, n=1418	-1.46 ± 10.65, n=1049	0.00076
Relative change [(FU - BL)/BL]	-0.00 ± 0.14, n=4085	0.01 ± 0.15, n=1618	-0.01 ± 0.14, n=1418	-0.01 ± 0.14, n=1049	0.00091
Weight [kg]	88.85 ± 18.11, n=4096	88.67 ± 18.21, n=1627	88.92 ± 17.65, n=1420	89.06 ± 18.58, n=1049	0.81647
Absolute change [FU - BL]	-1.27 ± 6.02, n=4096	-1.16 ± 6.10, n=1627	-1.36 ± 5.88, n=1420	-1.33 ± 6.09, n=1049	0.64659
Relative change [(FU - BL)/BL]	-0.01 ± 0.07, n=4096	-0.01 ± 0.07, n=1627	-0.01 ± 0.06, n=1420	-0.01 ± 0.07, n=1049	0.66936
BMI [kg/m2]	30.74 ± 5.74, n=4096	30.72 ± 5.85, n=1627	30.68 ± 5.58, n=1420	30.86 ± 5.79, n=1049	0.76163
Absolute change [FU - BL]	-0.43 ± 2.08, n=4096	-0.39 ± 2.12, n=1627	-0.47 ± 2.04, n=1420	-0.46 ± 2.08, n=1049	0.64733
Relative change [(FU - BL)/BL]	-0.01 ± 0.07, n=4096	-0.01 ± 0.07, n=1627	-0.01 ± 0.06, n=1420	-0.01 ± 0.07, n=1049	0.67083
BMI < 25	12.4 % (509/4096)	13.3 % (217/1627)	11.5 % (163/1420)	12.3 % (129/1049)	0.29695
BMI: 25 - 30	39.3 % (1608/4096)	38.5 % (626/1627)	41.3 % (587/1420)	37.7 % (395/1049)	0.12717

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
BMI > 30	48.3 % (1979/4096)	48.2 % (784/1627)	47.2 % (670/1420)	50.0 % (525/1049)	0.36781
Waist circumference [cm]	106.98 ± 16.18, n=1197	108.13 ± 15.62, n=453	104.94 ± 14.24, n=530	109.58 ± 20.71, n=214	0.00058
Absolute change [FU - BL]	-0.95 ± 9.45, n=1046	-1.03 ± 9.04, n=398	-1.58 ± 8.55, n=479	1.02 ± 12.22, n=169	0.05996
Relative change [(FU - BL)/BL]	-0.01 ± 0.09, n=1046	-0.01 ± 0.08, n=398	-0.01 ± 0.08, n=479	0.01 ± 0.11, n=169	0.03832
Diabetes training FU12+FU24	45.5 % (1874/4115)	51.0 % (834/1635)	44.6 % (637/1427)	38.3 % (403/1053)	<.00001
Participation in DMP diabetes	81.6 % (3345/4097)	83.0 % (1350/1626)	82.9 % (1178/1421)	77.8 % (817/1050)	0.00097

Table 9-70. *Absolute and relative changes in laboratory values in the SBP treatment groups at 24-month follow-up.*

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
No. of patients with FU data	4116 (100.0 %)	1636 (39.7 %)	1427 (34.7 %)	1053 (25.6 %)	
Total fasting cholesterol available	67.8 % (2792/4116)	64.2 % (1050/1636)	72.3 % (1032/1427)	67.4 % (710/1053)	<.00001
Total fasting cholesterol [mmol/L]	9.74 ± 3.05, n=2792	9.60 ± 3.06, n=1050	10.01 ± 2.83, n=1032	9.54 ± 3.32, n=710	0.00187
Absolute change [FU - BL]	4.42 ± 2.77, n=2646	4.37 ± 2.79, n=1005	4.68 ± 2.51, n=978	4.13 ± 3.06, n=663	0.00497
Relative change [(FU - BL)/BL]	0.87 ± 0.54, n=2646	0.87 ± 0.55, n=1005	0.92 ± 0.50, n=978	0.79 ± 0.58, n=663	0.00029
Fasting HDL-cholesterol available	52.3 % (2154/4116)	48.8 % (798/1636)	58.3 % (832/1427)	49.8 % (524/1053)	<.00001
Fasting HDL-cholesterol [mmol/L]	1.27 ± 0.36, n=2154	1.27 ± 0.34, n=798	1.28 ± 0.37, n=832	1.27 ± 0.37, n=524	0.42409
Absolute change [FU - BL]	0.02 ± 0.32, n=1986	0.03 ± 0.27, n=736	0.03 ± 0.35, n=764	0.01 ± 0.34, n=486	0.12336
Relative change [(FU - BL)/BL]	0.05 ± 0.29, n=1986	0.05 ± 0.23, n=736	0.06 ± 0.38, n=764	0.03 ± 0.21, n=486	0.11141
Fasting LDL-cholesterol available	50.9 % (2093/4116)	46.7 % (764/1636)	56.8 % (810/1427)	49.3 % (519/1053)	<.00001
Fasting LDL-cholesterol [mmol/L]	3.02 ± 0.93, n=2093	2.92 ± 0.94, n=764	3.04 ± 0.90, n=810	3.12 ± 0.93, n=519	0.00002
Absolute change [FU - BL]	-0.17 ± 0.82, n=1916	-0.16 ± 0.81, n=695	-0.16 ± 0.83, n=740	-0.21 ± 0.82, n=481	0.73864
Relative change [(FU - BL)/BL]	0.08 ± 1.90, n=1916	0.00 ± 0.47, n=695	0.18 ± 2.79, n=740	0.04 ± 1.42, n=481	0.89439
Fasting triglycerides available	59.1 % (2432/4116)	55.8 % (913/1636)	65.8 % (939/1427)	55.1 % (580/1053)	<.00001
Fasting triglycerides [mmol/L]	2.02 ± 1.19, n=2432	2.05 ± 1.25, n=913	1.94 ± 1.05, n=939	2.09 ± 1.31, n=580	0.02275
Absolute change [FU - BL]	-0.25 ± 1.35, n=2256	-0.20 ± 1.53, n=852	-0.25 ± 1.03, n=870	-0.34 ± 1.49, n=534	0.02044
Relative change [(FU - BL)/BL]	-0.00 ± 0.50, n=2256	0.04 ± 0.63, n=852	-0.03 ± 0.42, n=870	-0.04 ± 0.38, n=534	0.03203
Fasting glucose available	72.0 % (2965/4116)	70.6 % (1155/1636)	75.9 % (1083/1427)	69.0 % (727/1053)	0.00021
Fasting glucose [mmol/L]	7.31 ± 2.10, n=2965	7.21 ± 2.10, n=1155	7.28 ± 2.01, n=1083	7.52 ± 2.22, n=727	0.00005
Absolute change [FU - BL]	-1.12 ± 2.84, n=2808	-0.82 ± 2.73, n=1088	-1.37 ± 2.85, n=1038	-1.24 ± 2.94, n=682	<.00001
Relative change [(FU - BL)/BL]	-0.07 ± 0.50, n=2808	-0.05 ± 0.33, n=1088	-0.09 ± 0.71, n=1038	-0.09 ± 0.29, n=682	<.00001
Postprandial glucose available	40.1 % (1652/4116)	37.7 % (616/1636)	44.1 % (630/1427)	38.6 % (406/1053)	0.00059

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
Postprandial glucose [mmol/L]	8.64 ± 2.72, n=1652	8.81 ± 2.48, n=616	8.62 ± 2.44, n=630	8.41 ± 3.38, n=406	0.21789
Absolute change [FU - BL]	-2.27 ± 3.42, n=1372	-1.74 ± 3.29, n=521	-2.77 ± 3.36, n=551	-2.27 ± 3.60, n=300	<.00001
Relative change [(FU - BL)/BL]	-0.09 ± 1.20, n=1372	-0.12 ± 0.29, n=521	-0.08 ± 1.63, n=551	-0.06 ± 1.25, n=300	<.00001
HbA1c [%]	7.01 ± 0.99, n=3771	6.91 ± 0.98, n=1482	7.06 ± 0.99, n=1329	7.07 ± 0.98, n=960	<.00001
[HbA1c FU24 - target HbA1c]	0.12 ± 0.98, n=3771	0.24 ± 0.97, n=1482	0.12 ± 0.99, n=1329	-0.04 ± 0.95, n=960	<.00001
Target HbA1c met	55.7 % (2102/3771)	48.7 % (721/1482)	58.7 % (780/1329)	62.6 % (601/960)	<.00001
Absolute change [FU - BL]	-0.76 ± 1.34, n=3654	-0.61 ± 1.34, n=1434	-0.85 ± 1.36, n=1303	-0.85 ± 1.31, n=917	<.00001
Relative change [(FU - BL)/BL]	-0.08 ± 0.14, n=3654	-0.07 ± 0.14, n=1434	-0.09 ± 0.15, n=1303	-0.09 ± 0.14, n=917	<.00001
Haemoglobin available	46.6 % (1920/4116)	41.3 % (676/1636)	54.7 % (780/1427)	44.1 % (464/1053)	<.00001
Haemoglobin [mmol/L]	8.54 ± 1.11, n=1920	8.43 ± 1.13, n=676	8.66 ± 1.06, n=780	8.52 ± 1.14, n=464	0.00008
Absolute change [FU - BL]	-0.01 ± 0.74, n=1662	-0.02 ± 0.82, n=596	0.02 ± 0.72, n=665	-0.06 ± 0.66, n=401	0.00934
Relative change [(FU - BL)/BL]	0.00 ± 0.11, n=1662	0.01 ± 0.14, n=596	0.01 ± 0.10, n=665	-0.00 ± 0.08, n=401	0.00840
Serum creatinine available	72.0 % (2962/4116)	73.3 % (1200/1636)	75.2 % (1073/1427)	65.4 % (689/1053)	<.00001
Serum creatinine [µmol/l]	87.32 ± 146.70, n=2962	92.99 ± 228.01, n=1200	83.07 ± 29.81, n=1073	84.06 ± 23.31, n=689	0.02922
Absolute change [FU - BL]	0.28 ± 33.37, n=2715	0.59 ± 35.28, n=1113	0.04 ± 35.09, n=988	0.12 ± 26.24, n=614	0.06084
Relative change [(FU - BL)/BL]	0.03 ± 0.26, n=2715	0.04 ± 0.29, n=1113	0.02 ± 0.27, n=988	0.03 ± 0.20, n=614	0.08451
Microalbustix albumin [mg/l]	16.60 ± 31.16, n=897	17.74 ± 29.57, n=282	16.45 ± 31.73, n=423	15.24 ± 32.26, n=192	0.00096
Microalbustix creatinine [mg/dl]	38.19 ± 71.51, n=516	36.15 ± 67.34, n=165	54.89 ± 84.71, n=207	16.53 ± 44.71, n=144	0.00004
Macroalbuminuria: positive test	5.6 % (127/2249)	5.6 % (49/875)	5.2 % (42/815)	6.4 % (36/559)	0.59564
Macroalbuminuria: negative test	94.4 % (2122/2249)	94.4 % (826/875)	94.8 % (773/815)	93.6 % (523/559)	0.59564
Increased liver function readings	8.5 % (207/2445)	8.9 % (87/977)	7.2 % (64/884)	9.6 % (56/584)	0.23360

9.4.2.3 Therapeutic patterns

Therapeutic patterns at 6 months follow-up

Table 9-71 shows anti-diabetic therapy in the in the SBP treatment groups at 6-month follow-up (i.e. Metformin; Sulfonylurea drugs; Glucosidase inhibitors; Glinide; Glitazone; DPP-4 inhibitors; GLP-1 analogs; SGTL-2 inhibitors; Total number of antidiabetics; Insulin; Novartis drugs).

Table 9-72 shows anti-hypertensive therapy in the in the SBP treatment groups at 6-month follow-up (i.e. ACE inhibitors; ARB; Direct renin inhibitor; Beta-blocker; Calcium channel blocker; Diuretic drugs; Total number of antihypertensive drugs; Fixed-dose combinations; Novartis drugs).

Table 9-73 shows hypoglycemic events in the in the SBP treatment groups at 6-month follow-up (i.e. Number of events; Type of events; Help needed).

Table 9-71. *Anti-diabetic therapy in the SBP treatment groups at 6-month follow-up.*

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
No. of patients with FU data	7327 (100.0 %)	2836 (38.7 %)	2518 (34.4 %)	1973 (26.9 %)	
Metformin	79.7 % (5835/7321)	81.3 % (2301/2831)	80.4 % (2024/2517)	76.5 % (1510/1973)	0.00017
Metformin, dosage [mg/day]	1726.25 ± 527.95, n=5823	1695.32 ± 546.16, n=2290	1762.90 ± 505.30, n=2023	1724.03 ± 526.82, n=1510	0.00008
Sulfonylurea drugs	17.8 % (1302/7319)	16.1 % (455/2831)	18.6 % (467/2515)	19.3 % (380/1973)	0.00794
Sulfonylurea drugs, dosage [mg/day]	3.21 ± 1.93, n=1301	3.12 ± 1.87, n=454	3.24 ± 1.83, n=467	3.27 ± 2.11, n=380	0.32824
Substance					
Carbutamide	0.0 % (0/1301)	0.0 % (0/454)	0.0 % (0/467)	0.0 % (0/380)	
Tolbutamide	0.0 % (0/1301)	0.0 % (0/454)	0.0 % (0/467)	0.0 % (0/380)	
Glibenclamide	19.8 % (258/1301)	21.8 % (99/454)	18.8 % (88/467)	18.7 % (71/380)	0.42427
Glibornuride	0.0 % (0/1301)	0.0 % (0/454)	0.0 % (0/467)	0.0 % (0/380)	
Gliclazide	0.0 % (0/1301)	0.0 % (0/454)	0.0 % (0/467)	0.0 % (0/380)	
Glipizide	0.0 % (0/1301)	0.0 % (0/454)	0.0 % (0/467)	0.0 % (0/380)	
Gliquidone	0.4 % (5/1301)	0.2 % (1/454)	0.6 % (3/467)	0.3 % (1/380)	0.52800
Glisoxepide	0.1 % (1/1301)	0.2 % (1/454)	0.0 % (0/467)	0.0 % (0/380)	0.39316
Glycodiazine	0.8 % (11/1301)	1.3 % (6/454)	0.4 % (2/467)	0.8 % (3/380)	0.33098
Glimepiride	78.5 % (1021/1301)	76.0 % (345/454)	80.1 % (374/467)	79.5 % (302/380)	0.27254
Other	0.4 % (5/1301)	0.4 % (2/454)	0.0 % (0/467)	0.8 % (3/380)	0.17653
Glucosidase inhibitors	1.1 % (83/7321)	1.2 % (34/2832)	1.3 % (33/2516)	0.8 % (16/1973)	0.26487
Glucosidase inhibitors, dosage [mg/day]	144.30 ± 82.24, n=83	128.38 ± 66.82, n=34	157.94 ± 99.52, n=33	150.00 ± 70.71, n=16	0.47354
Substance					
Acarbose	91.6 % (76/83)	88.2 % (30/34)	93.9 % (31/33)	93.8 % (15/16)	0.66101
Miglitol	7.2 % (6/83)	8.8 % (3/34)	6.1 % (2/33)	6.3 % (1/16)	0.89631
Other	1.2 % (1/83)	2.9 % (1/34)	0.0 % (0/33)	0.0 % (0/16)	0.48221
Glinide	3.7 % (270/7311)	3.3 % (94/2822)	3.5 % (88/2516)	4.5 % (88/1973)	0.10151
Glinide, dosage [mg/day]	14.01 ± 54.81, n=269	23.88 ± 75.10, n=93	3.31 ± 2.72, n=88	14.28 ± 55.34, n=88	0.42438
Substance					
Nateglinide	3.0 % (8/270)	5.3 % (5/94)	0.0 % (0/88)	3.4 % (3/88)	0.10213
Repaglinide	93.7 % (253/270)	92.6 % (87/94)	97.7 % (86/88)	90.9 % (80/88)	0.15028
Other	3.3 % (9/270)	2.1 % (2/94)	2.3 % (2/88)	5.7 % (5/88)	0.32668
Glitazone	0.5 % (36/7321)	0.5 % (15/2832)	0.5 % (13/2516)	0.4 % (8/1973)	0.81249

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
Glitazone, dosage [mg/day]	38.64 ± 22.49, n=36	35.33 ± 21.75, n=15	38.08 ± 11.64, n=13	45.75 ± 35.62, n=8	0.63728
Substance					
Pioglitazon	86.1 % (31/36)	93.3 % (14/15)	100.0 % (13/13)	50.0 % (4/8)	0.00323
Other	13.9 % (5/36)	6.7 % (1/15)	0.0 % (0/13)	50.0 % (4/8)	0.00323
DPP-4 inhibitors	62.2 % (4543/7309)	60.9 % (1717/2819)	63.6 % (1600/2517)	62.1 % (1226/1973)	0.13540
DPP-4 inhibitors, dosage [mg/day]	84.88 ± 33.63, n=4543	85.15 ± 32.56, n=1717	84.68 ± 36.93, n=1600	84.75 ± 30.44, n=1226	0.93620
Substance					
Sitagliptin	30.0 % (1362/4543)	31.2 % (535/1717)	29.1 % (466/1600)	29.4 % (361/1226)	0.39434
Vildagliptin	65.2 % (2963/4543)	64.8 % (1113/1717)	65.4 % (1046/1600)	65.6 % (804/1226)	0.90198
Linagliptin	0.0 % (1/4543)	0.0 % (0/1717)	0.1 % (1/1600)	0.0 % (0/1226)	0.39856
Saxagliptin	4.4 % (202/4543)	3.6 % (62/1717)	5.3 % (84/1600)	4.6 % (56/1226)	0.07083
Other	0.3 % (15/4543)	0.4 % (7/1717)	0.2 % (3/1600)	0.4 % (5/1226)	0.46584
GLP-1 analogs/mimetics	5.4 % (394/7324)	5.4 % (152/2835)	5.5 % (139/2516)	5.2 % (103/1973)	0.90306
GLP-1 analogs/mimetics, dosage [mg/day]	6.95 ± 13.31, n=393	6.59 ± 11.47, n=152	5.52 ± 13.68, n=139	9.44 ± 15.04, n=102	0.01300
Substance					
Exenatide	39.4 % (155/393)	34.2 % (52/152)	36.0 % (50/139)	52.0 % (53/102)	0.01038
Liraglutide	53.2 % (209/393)	52.6 % (80/152)	59.7 % (83/139)	45.1 % (46/102)	0.07901
Other	7.4 % (29/393)	13.2 % (20/152)	4.3 % (6/139)	2.9 % (3/102)	0.00216
SGTL-2 inhibitors	2.1 % (154/7325)	1.9 % (55/2836)	2.0 % (51/2516)	2.4 % (48/1973)	0.47652
SGTL-2 inhibitors, dosage [mg/day]	13.14 ± 15.70, n=153	14.73 ± 18.34, n=55	11.86 ± 13.93, n=51	12.68 ± 14.28, n=47	0.02098
Substance					
Dapagliflozin	96.1 % (147/153)	96.4 % (53/55)	96.1 % (49/51)	95.7 % (45/47)	0.98720
Other	3.9 % (6/153)	3.6 % (2/55)	3.9 % (2/51)	4.3 % (2/47)	0.98720
Insulin(rapid-acting or long-acting or Pre-mixed)	17.1 % (1255/7327)	14.9 % (423/2836)	19.6 % (493/2518)	17.2 % (339/1973)	0.00004
Rapid-acting insulin	5.8 % (425/7325)	5.2 % (148/2836)	5.6 % (142/2516)	6.8 % (135/1973)	0.05534
Human insulin	45.9 % (195/425)	48.6 % (72/148)	35.9 % (51/142)	53.3 % (72/135)	0.01028
Analogues	54.1 % (230/425)	51.4 % (76/148)	64.1 % (91/142)	46.7 % (63/135)	0.01028
Syringe	3.1 % (13/425)	2.7 % (4/148)	3.5 % (5/142)	3.0 % (4/135)	0.91859
Pen	96.9 % (412/425)	97.3 % (144/148)	96.5 % (137/142)	97.0 % (131/135)	0.91859

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
Pump	0.0 % (0/425)	0.0 % (0/148)	0.0 % (0/142)	0.0 % (0/135)	
Other	0.0 % (0/425)	0.0 % (0/148)	0.0 % (0/142)	0.0 % (0/135)	
U-40	19.0 % (80/422)	22.4 % (33/147)	21.1 % (30/142)	12.8 % (17/133)	0.08617
U-100	81.0 % (342/422)	77.6 % (114/147)	78.9 % (112/142)	87.2 % (116/133)	0.08617
1x insulin/day	9.7 % (41/424)	10.9 % (16/147)	9.2 % (13/142)	8.9 % (12/135)	0.82465
2x insulin/day	14.9 % (63/424)	17.7 % (26/147)	12.0 % (17/142)	14.8 % (20/135)	0.39352
3x insulin/day	74.1 % (314/424)	70.7 % (104/147)	76.8 % (109/142)	74.8 % (101/135)	0.49209
4x insulin/day	1.4 % (6/424)	0.7 % (1/147)	2.1 % (3/142)	1.5 % (2/135)	0.58609
Long-acting insulin	15.8 % (1157/7325)	13.7 % (389/2836)	18.6 % (467/2516)	15.3 % (301/1973)	<.00001
Human insulin	29.9 % (346/1157)	31.6 % (123/389)	24.6 % (115/467)	35.9 % (108/301)	0.00263
Analogues	70.1 % (811/1157)	68.4 % (266/389)	75.4 % (352/467)	64.1 % (193/301)	0.00263
Syringe	5.3 % (61/1157)	5.7 % (22/389)	3.6 % (17/467)	7.3 % (22/301)	0.07789
Pen	94.5 % (1093/1157)	94.3 % (367/389)	95.9 % (448/467)	92.4 % (278/301)	0.10604
Pump	0.2 % (2/1157)	0.0 % (0/389)	0.2 % (1/467)	0.3 % (1/301)	0.55914
Other	0.1 % (1/1157)	0.0 % (0/389)	0.2 % (1/467)	0.0 % (0/301)	0.47740
U-40	15.3 % (176/1152)	18.5 % (72/389)	10.3 % (48/465)	18.8 % (56/298)	0.00061
U-100	84.7 % (976/1152)	81.5 % (317/389)	89.7 % (417/465)	81.2 % (242/298)	0.00061
1x insulin/day	86.0 % (995/1157)	85.9 % (334/389)	85.7 % (400/467)	86.7 % (261/301)	0.91428
2x insulin/day	12.4 % (144/1157)	12.9 % (50/389)	13.1 % (61/467)	11.0 % (33/301)	0.66065
3x insulin/day	1.5 % (17/1157)	1.0 % (4/389)	1.3 % (6/467)	2.3 % (7/301)	0.34013
4x insulin/day	0.1 % (1/1157)	0.3 % (1/389)	0.0 % (0/467)	0.0 % (0/301)	0.37232
Pre-mixed insulin	2.0 % (148/7325)	1.9 % (53/2836)	2.2 % (56/2516)	2.0 % (39/1973)	0.64271
Human insulin	61.5 % (91/148)	66.0 % (35/53)	64.3 % (36/56)	51.3 % (20/39)	0.30669
Analogues	38.5 % (57/148)	34.0 % (18/53)	35.7 % (20/56)	48.7 % (19/39)	0.30669
Syringe	4.1 % (6/148)	3.8 % (2/53)	3.6 % (2/56)	5.1 % (2/39)	0.92314
Pen	95.9 % (142/148)	96.2 % (51/53)	96.4 % (54/56)	94.9 % (37/39)	0.92314

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
Pump	0.0 % (0/148)	0.0 % (0/53)	0.0 % (0/56)	0.0 % (0/39)	
Other	0.0 % (0/148)	0.0 % (0/53)	0.0 % (0/56)	0.0 % (0/39)	
U-40	16.2 % (24/148)	22.6 % (12/53)	8.9 % (5/56)	17.9 % (7/39)	0.14330
U-100	83.8 % (124/148)	77.4 % (41/53)	91.1 % (51/56)	82.1 % (32/39)	0.14330
1x insulin/day	11.5 % (17/148)	9.4 % (5/53)	3.6 % (2/56)	25.6 % (10/39)	0.00342
2x insulin/day	85.1 % (126/148)	86.8 % (46/53)	91.1 % (51/56)	74.4 % (29/39)	0.07233
3x insulin/day	2.7 % (4/148)	3.8 % (2/53)	3.6 % (2/56)	0.0 % (0/39)	0.47827
4x insulin/day	0.7 % (1/148)	0.0 % (0/53)	1.8 % (1/56)	0.0 % (0/39)	0.43735
Fixed-dose combination metformin / DPP-4 inhibitor	76.2 % (2798/3672)	76.6 % (1078/1408)	76.0 % (991/1304)	75.9 % (729/960)	0.91937
Novartis drugs					
Vildagliptin / Metformin					
Eucreas	91.3 % (1786/1957)	92.2 % (674/731)	89.8 % (632/704)	92.0 % (480/522)	0.21413
Icandra	8.7 % (171/1957)	7.8 % (57/731)	10.2 % (72/704)	8.0 % (42/522)	0.21413
Vildagliptin					
Galvus	85.8 % (862/1005)	83.5 % (319/382)	86.0 % (294/342)	88.6 % (249/281)	0.17620
Jalra	14.2 % (143/1005)	16.5 % (63/382)	14.0 % (48/342)	11.4 % (32/281)	0.17620
Nateglinide					
STARLIX	100.0 % (8/8)	100.0 % (5/5)		100.0 % (3/3)	
Other	0.0 % (0/8)	0.0 % (0/5)		0.0 % (0/3)	

Table 9-72. *Anti-hypertensive therapy in the SBP treatment groups at 6-month follow-up.*

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
No. of patients with FU data	7327 (100.0 %)	2836 (38.7 %)	2518 (34.4 %)	1973 (26.9 %)	
ACE inhibitors	52.4 % (3838/7319)	50.6 % (1435/2835)	53.2 % (1336/2512)	54.1 % (1067/1972)	0.03813
ACE inhibitors, dosage [mg/day]	10.57 ± 12.53, n=3827	10.29 ± 12.40, n=1424	10.18 ± 11.62, n=1336	11.41 ± 13.71, n=1067	0.00238
Substance					
Captopril	2.6 % (100/3833)	3.0 % (43/1430)	2.2 % (30/1336)	2.5 % (27/1067)	0.44662
Enalapril	17.7 % (677/3833)	19.0 % (271/1430)	16.7 % (223/1336)	17.2 % (183/1067)	0.26046
Lisinopril	11.7 % (448/3833)	11.3 % (162/1430)	11.8 % (158/1336)	12.0 % (128/1067)	0.85990
Ramipril	65.0 % (2493/3833)	64.3 % (919/1430)	66.0 % (882/1336)	64.9 % (692/1067)	0.62031
Trandolapril	0.2 % (7/3833)	0.1 % (2/1430)	0.3 % (4/1336)	0.1 % (1/1067)	0.44809
Other	2.8 % (108/3833)	2.3 % (33/1430)	2.9 % (39/1336)	3.4 % (36/1067)	0.27060
Angiotensin receptor blocker (ARB)	28.3 % (2071/7314)	28.3 % (802/2830)	28.6 % (718/2512)	27.9 % (551/1972)	0.89345
ARB, dosage [mg/day]	116.35 ± 115.95, n=2068	118.00 ± 118.41, n=799	114.58 ± 115.55, n=718	116.28 ± 112.99, n=551	0.85649
Substance					
Candesartan	22.5 % (467/2071)	22.9 % (184/802)	22.7 % (163/718)	21.8 % (120/551)	0.87458
Irbesartan	5.6 % (115/2071)	6.0 % (48/802)	4.6 % (33/718)	6.2 % (34/551)	0.37913
Losartan	7.5 % (155/2071)	5.9 % (47/802)	8.2 % (59/718)	8.9 % (49/551)	0.07462
Valsartan	40.0 % (829/2071)	41.3 % (331/802)	40.0 % (287/718)	38.3 % (211/551)	0.54664
Other	24.4 % (505/2071)	23.9 % (192/802)	24.5 % (176/718)	24.9 % (137/551)	0.92268
Direct renin inhibitor	0.4 % (30/7313)	0.4 % (12/2829)	0.4 % (11/2512)	0.4 % (7/1972)	0.90125
Direct renin inhibitor, dosage [mg/day]	200.57 ± 89.72, n=30	188.83 ± 90.38, n=12	231.82 ± 78.33, n=11	171.57 ± 103.23, n=7	0.34823
Beta-blocker	47.9 % (3507/7317)	47.4 % (1343/2833)	48.8 % (1226/2512)	47.6 % (938/1972)	0.55188
Beta-blocker, dosage [mg/day]	54.08 ± 62.15, n=3500	53.36 ± 62.21, n=1336	57.02 ± 62.59, n=1226	51.25 ± 61.38, n=938	0.07779
Substance					
Metoprolol	45.6 % (1599/3506)	45.2 % (607/1342)	47.4 % (581/1226)	43.8 % (411/938)	0.23937
Bisoprolol	40.8 % (1430/3506)	41.4 % (556/1342)	38.8 % (476/1226)	42.4 % (398/938)	0.19861
Nebivolol	5.4 % (188/3506)	5.2 % (70/1342)	5.4 % (66/1226)	5.5 % (52/938)	0.94250

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
Carvedilol	4.8 % (169/3506)	4.5 % (60/1342)	5.2 % (64/1226)	4.8 % (45/938)	0.67520
Other	3.4 % (120/3506)	3.7 % (49/1342)	3.2 % (39/1226)	3.4 % (32/938)	0.80695
Calcium channel blocker	28.5 % (2082/7313)	25.9 % (732/2829)	28.7 % (720/2512)	31.9 % (630/1972)	0.00003
Calcium channel blocker, dosage [mg/day]	17.98 ± 42.62, n=2079	15.45 ± 34.00, n=729	19.19 ± 46.61, n=720	19.53 ± 46.56, n=630	0.57115
Substance					
Amlodipine	74.8 % (1558/2082)	74.5 % (545/732)	76.9 % (554/720)	72.9 % (459/630)	0.21586
Nifedipine	2.6 % (54/2082)	2.0 % (15/732)	2.5 % (18/720)	3.3 % (21/630)	0.32493
Nisoldipine	0.0 % (1/2082)	0.0 % (0/732)	0.1 % (1/720)	0.0 % (0/630)	0.38818
Nimodipine	0.0 % (1/2082)	0.1 % (1/732)	0.0 % (0/720)	0.0 % (0/630)	0.39749
Diltiazem	0.5 % (11/2082)	0.7 % (5/732)	0.0 % (0/720)	1.0 % (6/630)	0.04257
Verapamil	3.3 % (68/2082)	2.6 % (19/732)	3.1 % (22/720)	4.3 % (27/630)	0.20033
Gallopamil	0.0 % (0/2082)	0.0 % (0/732)	0.0 % (0/720)	0.0 % (0/630)	
Felodipine	3.0 % (63/2082)	2.9 % (21/732)	3.5 % (25/720)	2.7 % (17/630)	0.67687
Nitrendipine	4.3 % (89/2082)	4.4 % (32/732)	5.3 % (38/720)	3.0 % (19/630)	0.12082
Lercanidipine	10.2 % (213/2082)	11.2 % (82/732)	7.6 % (55/720)	12.1 % (76/630)	0.01558
Nilvadipine	0.0 % (1/2082)	0.1 % (1/732)	0.0 % (0/720)	0.0 % (0/630)	0.39749
Manidipine	0.0 % (1/2082)	0.1 % (1/732)	0.0 % (0/720)	0.0 % (0/630)	0.39749
Isradipine	0.1 % (2/2082)	0.3 % (2/732)	0.0 % (0/720)	0.0 % (0/630)	0.15786
Other	1.0 % (20/2082)	1.1 % (8/732)	1.0 % (7/720)	0.8 % (5/630)	0.85204
Diuretic drugs	43.7 % (3195/7316)	41.5 % (1175/2832)	42.7 % (1072/2512)	48.1 % (948/1972)	0.00002
Diuretic drugs, dosage [mg/day]	23.13 ± 23.63, n=3189	23.36 ± 24.52, n=1169	23.57 ± 25.90, n=1072	22.35 ± 19.46, n=948	0.86066
Substance					
Furosemide	8.6 % (275/3195)	8.3 % (98/1175)	8.2 % (88/1072)	9.4 % (89/948)	0.58934
Torasemide	23.5 % (750/3195)	23.0 % (270/1175)	23.1 % (248/1072)	24.5 % (232/948)	0.68539
Bumetanide	0.0 % (1/3195)	0.0 % (0/1175)	0.1 % (1/1072)	0.0 % (0/948)	0.37139
Etacrynic acid	0.0 % (1/3195)	0.0 % (0/1175)	0.1 % (1/1072)	0.0 % (0/948)	0.37139
Piretanide	1.1 % (35/3195)	1.4 % (16/1175)	1.1 % (12/1072)	0.7 % (7/948)	0.38869
Hydrochlorothiazide	68.7 % (2196/3195)	69.7 % (819/1175)	68.8 % (738/1072)	67.4 % (639/948)	0.52271
Clopamid	0.3 % (8/3195)	0.3 % (4/1175)	0.0 % (0/1072)	0.4 % (4/948)	0.12311
Other	8.6 % (274/3195)	8.3 % (98/1175)	9.1 % (98/1072)	8.2 % (78/948)	0.71626
Other anti-hypertensive therapy	10.5 % (769/7303)	9.3 % (261/2819)	10.9 % (275/2512)	11.8 % (233/1972)	0.01253

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
Fixed-dose combinations					
Fixed-dose combination ARB/calcium channel blocker/diuretic	71.5 % (432/604)	67.3 % (142/211)	73.9 % (150/203)	73.7 % (140/190)	0.24127
Fixed-dose combination ACE inhibitor/diuretic	49.4 % (802/1625)	49.0 % (283/577)	50.6 % (279/551)	48.3 % (240/497)	0.73755
Fixed-dose combination ARB/diuretic	64.0 % (533/833)	62.8 % (209/333)	62.8 % (172/274)	67.3 % (152/226)	0.48674
Fixed-dose combination ARB/calcium channel blocker	38.6 % (179/464)	39.6 % (72/182)	41.5 % (71/171)	32.4 % (36/111)	0.29110
Fixed-dose combination ACE inhibitor/calcium channel blocker	14.0 % (137/979)	13.5 % (45/334)	12.7 % (41/324)	15.9 % (51/321)	0.46882
Fixed-dose combination direct renin inhibitor/diuretic	52.6 % (10/19)	37.5 % (3/8)	50.0 % (4/8)	100.0 % (3/3)	0.17756
Novartis drugs					
Valsartan / Hydrochlorothiazide					
CoDiovan	30.5 % (57/187)	34.2 % (27/79)	28.1 % (18/64)	27.3 % (12/44)	0.64060
Codiovan forte	13.9 % (26/187)	10.1 % (8/79)	17.2 % (11/64)	15.9 % (7/44)	0.43477
Cordinate plus	1.6 % (3/187)	2.5 % (2/79)	1.6 % (1/64)	0.0 % (0/44)	0.56313
Provas	0.5 % (1/187)	0.0 % (0/79)	1.6 % (1/64)	0.0 % (0/44)	0.38056
Provas comp	5.9 % (11/187)	6.3 % (5/79)	7.8 % (5/64)	2.3 % (1/44)	0.47363
Provas maxx	1.6 % (3/187)	2.5 % (2/79)	0.0 % (0/64)	2.3 % (1/44)	0.44968
Other	46.0 % (86/187)	44.3 % (35/79)	43.8 % (28/64)	52.3 % (23/44)	0.63162
Valsartan					
Cordinate	3.3 % (10/299)	1.6 % (2/129)	3.1 % (3/98)	6.9 % (5/72)	0.12274
Diovan	33.4 % (100/299)	33.3 % (43/129)	29.6 % (29/98)	38.9 % (28/72)	0.44642
Provas	6.7 % (20/299)	3.9 % (5/129)	5.1 % (5/98)	13.9 % (10/72)	0.01822
Other	56.5 % (169/299)	61.2 % (79/129)	62.2 % (61/98)	40.3 % (29/72)	0.00608
Valsartan / Amlodipine / Hydrochlorothiazide					
Exforge HCT	76.8 % (159/207)	82.7 % (62/75)	80.3 % (57/71)	65.6 % (40/61)	0.04397
Dafiro HCT	12.6 % (26/207)	8.0 % (6/75)	12.7 % (9/71)	18.0 % (11/61)	0.21391
Other	10.6 % (22/207)	9.3 % (7/75)	7.0 % (5/71)	16.4 % (10/61)	0.19907
Aliskiren					
Rasilez	95.0 % (19/20)	100.0 % (9/9)	100.0 % (7/7)	75.0 % (3/4)	0.12181
Other	5.0 % (1/20)	0.0 % (0/9)	0.0 % (0/7)	25.0 % (1/4)	0.12181
Hydrochlorothiazide					
Esidrix	4.0 % (22/552)	6.2 % (14/227)	2.4 % (4/169)	2.6 % (4/156)	0.09050
Other	96.0 % (530/552)	93.8 % (213/227)	97.6 % (165/169)	97.4 % (152/156)	0.09050

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
Aliskiren / Hydrochlorothiazide					
Rasilez HCT	90.0 % (9/10)	66.7 % (2/3)	100.0 % (4/4)	100.0 % (3/3)	0.27354
Other	10.0 % (1/10)	33.3 % (1/3)	0.0 % (0/4)	0.0 % (0/3)	0.27354
Valsartan / Amlodipine					
Exforge	81.4 % (83/102)	77.5 % (31/40)	83.7 % (36/43)	84.2 % (16/19)	0.72139
Dafiro	15.7 % (16/102)	17.5 % (7/40)	16.3 % (7/43)	10.5 % (2/19)	0.78137
Other	2.9 % (3/102)	5.0 % (2/40)	0.0 % (0/43)	5.3 % (1/19)	0.32371

Table 9-73. *Hypoglycemic events in the SBP treatment groups at 6-month follow-up.*

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
No. of patients with FU data	7327 (100.0 %)	2836 (38.7 %)	2518 (34.4 %)	1973 (26.9 %)	
Hypoglycemic events since baseline					
Without specific symptoms	0.4 % (25/7128)	0.3 % (9/2781)	0.3 % (8/2469)	0.4 % (8/1878)	0.81335
No. of events	2.28 ± 1.65, n=25	2.22 ± 1.72, n=9	1.88 ± 0.83, n=8	2.75 ± 2.19, n=8	0.59521
Symptomatic, but controllable without external help	0.4 % (26/7184)	0.3 % (7/2796)	0.2 % (6/2487)	0.7 % (13/1901)	0.02432
No. of events	2.46 ± 3.02, n=26	2.00 ± 1.53, n=7	1.83 ± 0.75, n=6	3.00 ± 4.12, n=13	0.95152
External help needed	0.0 % (2/7193)	0.0 % (0/2798)	0.0 % (1/2487)	0.1 % (1/1908)	0.51390
No. of events	1.00 ± 0.00, n=2	, n=0	1.00, n=1	1.00, n=1	
Symptomatic with medical help	0.0 % (1/7192)	0.0 % (0/2798)	0.0 % (1/2485)	0.0 % (0/1909)	0.38782
No. of events	1.00, n=1	, n=0	1.00, n=1	, n=0	
Hospitalization required	0.0 % (1/7201)	0.0 % (0/2798)	0.0 % (1/2490)	0.0 % (0/1913)	0.38825
No. of events	1.00, n=1	, n=0	1.00, n=1	, n=0	

Therapeutic patterns at 12 months follow-up

Table 9-74 shows anti-diabetic therapy in the in the SBP treatment groups at 12-month follow-up (i.e. Metformin; Sulfonylurea drugs; Glucosidase inhibitors; Glinide; Glitazone; DPP-4 inhibitors; GLP-1 analogs; SGTL-2 inhibitors; Total number of antidiabetics; Insulin; Novartis drugs).

Table 9-75 shows anti-hypertensive therapy in the in the SBP treatment groups at 12-month follow-up (i.e. ACE inhibitors; ARB; Direct renin inhibitor; Beta-blocker; Calcium channel blocker; Diuretic drugs; Total number of antihypertensive drugs; Fixed-dose combinations; Novartis drugs).

Table 9-76 shows hypoglycemic events in the in the SBP treatment groups at 12-month follow-up (i.e. Number of events; Type of events; Help needed).

Table 9-74. *Anti-diabetic therapy in the SBP treatment group at 12-month follow-up.*

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
No. of patients with FU data	6666 (100.0 %)	2632 (39.5 %)	2311 (34.7 %)	1723 (25.8 %)	
Metformin	79.8 % (5318/6666)	80.5 % (2118/2632)	81.3 % (1878/2311)	76.7 % (1322/1723)	0.00096
Metformin, dosage [mg/day]	1737.78 ± 515.82, n=5318	1706.39 ± 531.76, n=2118	1769.26 ± 497.51, n=1878	1743.37 ± 512.90, n=1322	0.00098
Sulfonylurea drugs	17.6 % (1175/6664)	15.7 % (413/2632)	18.1 % (419/2309)	19.9 % (343/1723)	0.00124
Sulfonylurea drugs, dosage [mg/day]	3.17 ± 1.91, n=1175	3.14 ± 1.93, n=413	3.23 ± 1.79, n=419	3.14 ± 2.03, n=343	0.13325
Substance					
Carbutamide	0.0 % (0/1175)	0.0 % (0/413)	0.0 % (0/419)	0.0 % (0/343)	
Tolbutamide	0.0 % (0/1175)	0.0 % (0/413)	0.0 % (0/419)	0.0 % (0/343)	
Glibenclamide	18.8 % (221/1175)	21.1 % (87/413)	18.1 % (76/419)	16.9 % (58/343)	0.31496
Glibornuride	0.0 % (0/1175)	0.0 % (0/413)	0.0 % (0/419)	0.0 % (0/343)	
Gliclazide	0.0 % (0/1175)	0.0 % (0/413)	0.0 % (0/419)	0.0 % (0/343)	
Glipizide	0.0 % (0/1175)	0.0 % (0/413)	0.0 % (0/419)	0.0 % (0/343)	
Gliquidone	0.4 % (5/1175)	0.5 % (2/413)	0.5 % (2/419)	0.3 % (1/343)	0.90237
Glisoxepide	0.0 % (0/1175)	0.0 % (0/413)	0.0 % (0/419)	0.0 % (0/343)	
Glycodiazine	0.5 % (6/1175)	0.7 % (3/413)	0.2 % (1/419)	0.6 % (2/343)	0.59931
Glimepiride	79.7 % (937/1175)	77.2 % (319/413)	81.1 % (340/419)	81.0 % (278/343)	0.29010
Other	0.5 % (6/1175)	0.5 % (2/413)	0.0 % (0/419)	1.2 % (4/343)	0.07975
Glucosidase inhibitors	1.2 % (78/6665)	1.3 % (33/2632)	1.3 % (30/2310)	0.9 % (15/1723)	0.40127
Glucosidase inhibitors, dosage [mg/day]	148.42 ± 79.73, n=78	127.73 ± 57.79, n=33	168.73 ± 97.99, n=30	153.33 ± 74.32, n=15	0.21180
Substance					
Acarbose	92.3 % (72/78)	87.9 % (29/33)	93.3 % (28/30)	100.0 % (15/15)	0.33186
Miglitol	6.4 % (5/78)	9.1 % (3/33)	6.7 % (2/30)	0.0 % (0/15)	0.49018
Other	1.3 % (1/78)	3.0 % (1/33)	0.0 % (0/30)	0.0 % (0/15)	0.50124
Glinide	3.9 % (261/6665)	3.6 % (96/2632)	3.8 % (87/2310)	4.5 % (78/1723)	0.30855
Glinide, dosage [mg/day]	14.96 ± 58.99, n=261	22.19 ± 73.30, n=96	7.37 ± 38.34, n=87	14.53 ± 57.87, n=78	0.17888
Substance					
Nateglinide	3.4 % (9/261)	5.2 % (5/96)	1.1 % (1/87)	3.8 % (3/78)	0.31486
Repaglinide	94.6 % (247/261)	93.8 % (90/96)	96.6 % (84/87)	93.6 % (73/78)	0.62324
Other	1.9 % (5/261)	1.0 % (1/96)	2.3 % (2/87)	2.6 % (2/78)	0.72877
Glitazone	0.5 % (34/6665)	0.6 % (15/2632)	0.6 % (14/2310)	0.3 % (5/1723)	0.32524

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
Glitazone, dosage [mg/day]	39.44 ± 22.67, n=34	37.00 ± 20.16, n=15	36.43 ± 12.77, n=14	55.20 ± 43.85, n=5	0.64350
Substance					
Pioglitazon	85.3 % (29/34)	93.3 % (14/15)	100.0 % (14/14)	20.0 % (1/5)	0.00004
Other	14.7 % (5/34)	6.7 % (1/15)	0.0 % (0/14)	80.0 % (4/5)	0.00004
DPP-4 inhibitors	61.9 % (4126/6666)	60.7 % (1598/2632)	63.2 % (1460/2311)	62.0 % (1068/1723)	0.20496
DPP-4 inhibitors, dosage [mg/day]	84.55 ± 31.31, n=4126	85.72 ± 32.74, n=1598	83.15 ± 30.02, n=1460	84.71 ± 30.80, n=1068	0.52668
Substance					
Sitagliptin	31.7 % (1307/4126)	31.9 % (510/1598)	30.5 % (446/1460)	32.9 % (351/1068)	0.44969
Vildagliptin	63.0 % (2600/4126)	64.0 % (1023/1598)	62.9 % (919/1460)	61.6 % (658/1068)	0.45020
Linagliptin	0.0 % (0/4126)	0.0 % (0/1598)	0.0 % (0/1460)	0.0 % (0/1068)	
Saxagliptin	5.0 % (206/4126)	3.6 % (58/1598)	6.3 % (92/1460)	5.2 % (56/1068)	0.00292
Other	0.3 % (13/4126)	0.4 % (7/1598)	0.2 % (3/1460)	0.3 % (3/1068)	0.50473
GLP-1 analogs/mimetics	5.1 % (343/6665)	5.2 % (136/2632)	5.4 % (124/2310)	4.8 % (83/1723)	0.73447
GLP-1 analogs/mimetics, dosage [mg/day]	7.15 ± 14.01, n=343	6.83 ± 11.88, n=136	5.88 ± 14.40, n=124	9.56 ± 16.34, n=83	0.03782
Substance					
Exenatide	39.4 % (135/343)	34.6 % (47/136)	37.9 % (47/124)	49.4 % (41/83)	0.08512
Liraglutide	54.5 % (187/343)	54.4 % (74/136)	58.1 % (72/124)	49.4 % (41/83)	0.47066
Other	6.1 % (21/343)	11.0 % (15/136)	4.0 % (5/124)	1.2 % (1/83)	0.00631
SGTL-2 inhibitors	2.5 % (169/6665)	2.2 % (58/2632)	2.8 % (64/2310)	2.7 % (47/1723)	0.37773
SGTL-2 inhibitors, dosage [mg/day]	11.99 ± 14.15, n=169	11.38 ± 11.88, n=58	13.59 ± 19.38, n=64	10.55 ± 5.99, n=47	0.54992
Substance					
Dapagliflozin	95.9 % (162/169)	98.3 % (57/58)	92.2 % (59/64)	97.9 % (46/47)	0.17326
Other	4.1 % (7/169)	1.7 % (1/58)	7.8 % (5/64)	2.1 % (1/47)	0.17326
Insulin(rapid-acting or long-acting or Pre-mixed)	19.7 % (1310/6666)	16.8 % (443/2632)	22.5 % (519/2311)	20.2 % (348/1723)	<.00001
Rapid-acting insulin	6.9 % (462/6665)	6.1 % (161/2632)	7.0 % (161/2310)	8.1 % (140/1723)	0.03842
Human insulin	42.9 % (198/462)	46.6 % (75/161)	32.3 % (52/161)	50.7 % (71/140)	0.00278
Analogues	57.1 % (264/462)	53.4 % (86/161)	67.7 % (109/161)	49.3 % (69/140)	0.00278
Syringe	3.7 % (17/462)	3.1 % (5/161)	3.1 % (5/161)	5.0 % (7/140)	0.61018
Pen	96.3 % (445/462)	96.9 % (156/161)	96.9 % (156/161)	95.0 % (133/140)	0.61018

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
Pump	0.0 % (0/462)	0.0 % (0/161)	0.0 % (0/161)	0.0 % (0/140)	
Other	0.0 % (0/462)	0.0 % (0/161)	0.0 % (0/161)	0.0 % (0/140)	
U-40	15.4 % (71/460)	17.4 % (28/161)	15.5 % (25/161)	13.0 % (18/138)	0.58338
U-100	84.6 % (389/460)	82.6 % (133/161)	84.5 % (136/161)	87.0 % (120/138)	0.58338
1x insulin/day	9.3 % (43/462)	11.8 % (19/161)	7.5 % (12/161)	8.6 % (12/140)	0.38067
2x insulin/day	13.4 % (62/462)	14.9 % (24/161)	14.3 % (23/161)	10.7 % (15/140)	0.52406
3x insulin/day	76.0 % (351/462)	72.0 % (116/161)	76.4 % (123/161)	80.0 % (112/140)	0.27018
4x insulin/day	1.3 % (6/462)	1.2 % (2/161)	1.9 % (3/161)	0.7 % (1/140)	0.67791
Long-acting insulin	18.3 % (1222/6665)	15.6 % (411/2632)	21.3 % (492/2310)	18.5 % (319/1723)	<.00001
Human insulin	29.1 % (356/1222)	30.7 % (126/411)	24.8 % (122/492)	33.9 % (108/319)	0.01507
Analogues	70.9 % (866/1222)	69.3 % (285/411)	75.2 % (370/492)	66.1 % (211/319)	0.01507
Syringe	5.8 % (71/1222)	7.1 % (29/411)	2.8 % (14/492)	8.8 % (28/319)	0.00083
Pen	93.9 % (1147/1222)	92.7 % (381/411)	96.7 % (476/492)	90.9 % (290/319)	0.00158
Pump	0.2 % (2/1222)	0.0 % (0/411)	0.2 % (1/492)	0.3 % (1/319)	0.56014
Other	0.2 % (2/1222)	0.2 % (1/411)	0.2 % (1/492)	0.0 % (0/319)	0.69431
U-40	15.4 % (187/1218)	19.5 % (80/410)	10.4 % (51/491)	17.7 % (56/317)	0.00032
U-100	84.6 % (1031/1218)	80.5 % (330/410)	89.6 % (440/491)	82.3 % (261/317)	0.00032
1x insulin/day	86.2 % (1053/1222)	86.1 % (354/411)	85.8 % (422/492)	86.8 % (277/319)	0.91221
2x insulin/day	12.3 % (150/1222)	12.7 % (52/411)	12.8 % (63/492)	11.0 % (35/319)	0.70975
3x insulin/day	1.5 % (18/1222)	1.0 % (4/411)	1.4 % (7/492)	2.2 % (7/319)	0.39463
4x insulin/day	0.1 % (1/1222)	0.2 % (1/411)	0.0 % (0/492)	0.0 % (0/319)	0.37253
Pre-mixed insulin	2.3 % (154/6665)	2.1 % (55/2632)	2.7 % (62/2310)	2.1 % (37/1723)	0.33300
Human insulin	65.6 % (101/154)	70.9 % (39/55)	66.1 % (41/62)	56.8 % (21/37)	0.37224
Analogues	34.4 % (53/154)	29.1 % (16/55)	33.9 % (21/62)	43.2 % (16/37)	0.37224

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
Syringe	5.2 % (8/153)	3.6 % (2/55)	6.6 % (4/61)	5.4 % (2/37)	0.77838
Pen	94.8 % (145/153)	96.4 % (53/55)	93.4 % (57/61)	94.6 % (35/37)	0.77838
Pump	0.0 % (0/153)	0.0 % (0/55)	0.0 % (0/61)	0.0 % (0/37)	
Other	0.0 % (0/153)	0.0 % (0/55)	0.0 % (0/61)	0.0 % (0/37)	
U-40	15.8 % (24/152)	21.8 % (12/55)	8.2 % (5/61)	19.4 % (7/36)	0.10488
U-100	84.2 % (128/152)	78.2 % (43/55)	91.8 % (56/61)	80.6 % (29/36)	0.10488
1x insulin/day	10.5 % (16/153)	9.1 % (5/55)	6.6 % (4/61)	18.9 % (7/37)	0.14019
2x insulin/day	84.3 % (129/153)	85.5 % (47/55)	86.9 % (53/61)	78.4 % (29/37)	0.51052
3x insulin/day	4.6 % (7/153)	5.5 % (3/55)	4.9 % (3/61)	2.7 % (1/37)	0.81425
4x insulin/day	0.7 % (1/153)	0.0 % (0/55)	1.6 % (1/61)	0.0 % (0/37)	0.46811
Fixed-dose combination metformin / DPP-4 inhibitor	78.1 % (2635/3374)	77.5 % (1017/1313)	78.2 % (948/1213)	79.0 % (670/848)	0.69414
Novartis drugs					
Vildagliptin / Metformin					
Eucreas	91.8 % (1626/1772)	92.6 % (626/676)	90.6 % (586/647)	92.2 % (414/449)	0.37496
Icandra	8.2 % (146/1772)	7.4 % (50/676)	9.4 % (61/647)	7.8 % (35/449)	0.37496
Vildagliptin					
Galvus	85.0 % (704/828)	83.6 % (290/347)	84.9 % (231/272)	87.6 % (183/209)	0.44245
Jalra	15.0 % (124/828)	16.4 % (57/347)	15.1 % (41/272)	12.4 % (26/209)	0.44245
Nateglinide					
STARLIX	100.0 % (9/9)	100.0 % (5/5)	100.0 % (1/1)	100.0 % (3/3)	
Other	0.0 % (0/9)	0.0 % (0/5)	0.0 % (0/1)	0.0 % (0/3)	

Table 9-75. *Anti-hypertensive therapy in the SBP treatment groups at 12-month follow-up.*

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
No. of patients with FU data	6666 (100.0 %)	2632 (39.5 %)	2311 (34.7 %)	1723 (25.8 %)	
ACE inhibitors	52.1 % (3471/6665)	49.9 % (1314/2632)	53.2 % (1228/2310)	53.9 % (929/1723)	0.01566
ACE inhibitors, dosage [mg/day]	10.0 (5.0, 10.0)	7.5 (5.0, 10.0)	7.5 (5.0, 10.0)	10.0 (5.0, 10.0)	0.05168
Substance					
Captopril	2.4 % (83/3471)	2.7 % (36/1314)	2.1 % (26/1228)	2.3 % (21/929)	0.56365
Enalapril	17.7 % (614/3471)	20.2 % (265/1314)	16.0 % (197/1228)	16.4 % (152/929)	0.01137
Lisinopril	11.8 % (411/3471)	11.8 % (155/1314)	11.6 % (143/1228)	12.2 % (113/929)	0.93221
Ramipril	64.9 % (2254/3471)	62.8 % (825/1314)	66.9 % (821/1228)	65.4 % (608/929)	0.09231
Trandolapril	0.2 % (6/3471)	0.2 % (2/1314)	0.2 % (3/1228)	0.1 % (1/929)	0.73174
Other	3.0 % (103/3471)	2.4 % (31/1314)	3.1 % (38/1228)	3.7 % (34/929)	0.19168
Angiotensin receptor blocker (ARB)	28.8 % (1922/6665)	28.9 % (760/2632)	29.4 % (679/2310)	28.0 % (483/1723)	0.63940
ARB, dosage [mg/day]	80.0 (20.0, 160.0)	80.0 (25.0, 160.0)	80.0 (20.0, 160.0)	80.0 (20.0, 160.0)	0.81125
Substance					
Candesartan	23.2 % (445/1922)	23.2 % (176/760)	23.7 % (161/679)	22.4 % (108/483)	0.86520
Irbesartan	5.5 % (106/1922)	5.7 % (43/760)	4.9 % (33/679)	6.2 % (30/483)	0.59515
Losartan	7.3 % (140/1922)	5.8 % (44/760)	7.7 % (52/679)	9.1 % (44/483)	0.08053
Valsartan	39.9 % (766/1922)	40.8 % (310/760)	39.9 % (271/679)	38.3 % (185/483)	0.68264
Other	24.2 % (465/1922)	24.6 % (187/760)	23.9 % (162/679)	24.0 % (116/483)	0.94175
Direct renin inhibitor	0.4 % (26/6665)	0.4 % (10/2632)	0.5 % (11/2310)	0.3 % (5/1723)	0.64076
Direct renin inhibitor, dosage [mg/day]	150.0 (150.0, 300.0)	150.0 (150.0, 300.0)	300.0 (150.0, 300.0)	150.0 (150.0, 150.0)	0.15589
Beta-blocker	48.7 % (3246/6665)	48.2 % (1269/2632)	49.3 % (1139/2310)	48.6 % (838/1723)	0.74363
Beta-blocker, dosage [mg/day]	25.0 (5.0, 95.0)	25.0 (5.0, 95.0)	25.0 (5.0, 95.0)	10.0 (5.0, 95.0)	0.05479
Substance					
Metoprolol	45.0 % (1460/3246)	45.0 % (571/1269)	47.0 % (535/1139)	42.2 % (354/838)	0.11302

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
Bisoprolol	41.4 % (1345/3246)	41.8 % (531/1269)	39.4 % (449/1139)	43.6 % (365/838)	0.16984
Nebivolol	5.5 % (180/3246)	5.4 % (69/1269)	5.6 % (64/1139)	5.6 % (47/838)	0.97705
Carvedilol	4.7 % (152/3246)	4.4 % (56/1269)	5.1 % (58/1139)	4.5 % (38/838)	0.71320
Other	3.4 % (109/3246)	3.3 % (42/1269)	2.9 % (33/1139)	4.1 % (34/838)	0.36480
Calcium channel blocker	29.1 % (1939/6665)	26.3 % (692/2632)	29.4 % (680/2310)	32.9 % (567/1723)	0.00001
Calcium channel blocker, dosage [mg/day]	10.0 (5.0, 10.0)	10.0 (5.0, 10.0)	10.0 (5.0, 10.0)	10.0 (5.0, 10.0)	0.91085
Substance					
Amlodipine	75.1 % (1457/1939)	74.0 % (512/692)	77.2 % (525/680)	74.1 % (420/567)	0.30272
Nifedipine	2.2 % (42/1939)	1.7 % (12/692)	2.6 % (18/680)	2.1 % (12/567)	0.50705
Nisoldipine	0.1 % (1/1939)	0.0 % (0/692)	0.1 % (1/680)	0.0 % (0/567)	0.39605
Nimodipine	0.1 % (1/1939)	0.1 % (1/692)	0.0 % (0/680)	0.0 % (0/567)	0.40597
Diltiazem	0.6 % (12/1939)	0.7 % (5/692)	0.0 % (0/680)	1.2 % (7/567)	0.01974
Verapamil	3.3 % (64/1939)	2.6 % (18/692)	3.2 % (22/680)	4.2 % (24/567)	0.27069
Gallopamil	0.0 % (0/1939)	0.0 % (0/692)	0.0 % (0/680)	0.0 % (0/567)	
Felodipine	3.0 % (58/1939)	3.0 % (21/692)	3.2 % (22/680)	2.6 % (15/567)	0.82793
Nitrendipine	4.1 % (80/1939)	4.2 % (29/692)	5.1 % (35/680)	2.8 % (16/567)	0.12018
Lercanidipine	10.4 % (202/1939)	11.8 % (82/692)	7.4 % (50/680)	12.3 % (70/567)	0.00493
Nilvadipine	0.1 % (1/1939)	0.1 % (1/692)	0.0 % (0/680)	0.0 % (0/567)	0.40597
Manidipine	0.1 % (1/1939)	0.1 % (1/692)	0.0 % (0/680)	0.0 % (0/567)	0.40597
Isradipine	0.1 % (2/1939)	0.3 % (2/692)	0.0 % (0/680)	0.0 % (0/567)	0.16466
Other	0.9 % (18/1939)	1.2 % (8/692)	1.0 % (7/680)	0.5 % (3/567)	0.48471
Diuretic drugs	44.2 % (2943/6665)	41.8 % (1100/2632)	43.9 % (1013/2310)	48.2 % (830/1723)	0.00017
Diuretic drugs, dosage [mg/day]	20.0 (12.5, 25.0)	20.0 (12.5, 25.0)	20.0 (12.5, 25.0)	16.3 (12.5, 25.0)	0.88319
Substance					
Furosemide	8.4 % (247/2943)	8.1 % (89/1100)	7.9 % (80/1013)	9.4 % (78/830)	0.46214
Torasemide	23.3 % (687/2943)	22.8 % (251/1100)	23.5 % (238/1013)	23.9 % (198/830)	0.85894

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
Bumetanide	0.0 % (1/2943)	0.0 % (0/1100)	0.1 % (1/1013)	0.0 % (0/830)	0.38561
Etacrynic acid	0.0 % (1/2943)	0.0 % (0/1100)	0.1 % (1/1013)	0.0 % (0/830)	0.38561
Piretanide	1.1 % (32/2943)	1.5 % (16/1100)	1.1 % (11/1013)	0.6 % (5/830)	0.20251
Hydrochlorothiazide	69.7 % (2051/2943)	70.8 % (779/1100)	69.2 % (701/1013)	68.8 % (571/830)	0.57914
Clopamid	0.2 % (7/2943)	0.3 % (3/1100)	0.0 % (0/1013)	0.5 % (4/830)	0.10252
Other	8.4 % (248/2943)	8.2 % (90/1100)	8.9 % (90/1013)	8.2 % (68/830)	0.81080
Other anti-hypertensive therapy	10.7 % (716/6665)	9.9 % (261/2632)	10.9 % (251/2310)	11.8 % (204/1723)	0.13045
Fixed-dose combinations					
Fixed-dose combination ARB/calcium channel blocker/diuretic	72.6 % (418/576)	69.3 % (147/212)	72.1 % (142/197)	77.2 % (129/167)	0.22662
Fixed-dose combination ACE inhibitor/diuretic	49.9 % (738/1478)	50.5 % (267/529)	50.0 % (259/518)	49.2 % (212/431)	0.92393
Fixed-dose combination ARB/diuretic	65.1 % (504/774)	64.7 % (205/317)	63.2 % (168/266)	68.6 % (131/191)	0.47483
Fixed-dose combination ARB/calcium channel blocker	39.5 % (169/428)	39.8 % (66/166)	39.8 % (66/166)	38.5 % (37/96)	0.97717
Fixed-dose combination ACE inhibitor/calcium channel blocker	16.0 % (146/910)	15.3 % (47/307)	15.1 % (47/311)	17.8 % (52/292)	0.60713
Fixed-dose combination direct renin inhibitor/diuretic	50.0 % (8/16)	33.3 % (2/6)	50.0 % (4/8)	100.0 % (2/2)	0.26360
Novartis drugs					
Valsartan / Hydrochlorothiazide					
CoDiovan	31.4 % (54/172)	37.3 % (28/75)	27.6 % (16/58)	25.6 % (10/39)	0.32988
Codiovan forte	13.4 % (23/172)	10.7 % (8/75)	17.2 % (10/58)	12.8 % (5/39)	0.53963
Cordinate plus	1.7 % (3/172)	2.7 % (2/75)	1.7 % (1/58)	0.0 % (0/39)	0.58718
Provas	0.6 % (1/172)	0.0 % (0/75)	1.7 % (1/58)	0.0 % (0/39)	0.37213
Provas comp	5.2 % (9/172)	5.3 % (4/75)	6.9 % (4/58)	2.6 % (1/39)	0.64229
Provas maxx	1.7 % (3/172)	2.7 % (2/75)	0.0 % (0/58)	2.6 % (1/39)	0.45956
Other	45.9 % (79/172)	41.3 % (31/75)	44.8 % (26/58)	56.4 % (22/39)	0.30250
Valsartan					
Cordinate	1.5 % (4/260)	0.9 % (1/110)	0.0 % (0/93)	5.3 % (3/57)	0.03079
Diovan	27.7 % (72/260)	26.4 % (29/110)	28.0 % (26/93)	29.8 % (17/57)	0.89152

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
Provas	7.3 % (19/260)	4.5 % (5/110)	5.4 % (5/93)	15.8 % (9/57)	0.02019
Other	63.5 % (165/260)	68.2 % (75/110)	66.7 % (62/93)	49.1 % (28/57)	0.03833
Valsartan / Amlodipine / Hydrochlorothiazide					
Exforge HCT	76.6 % (160/209)	78.8 % (63/80)	80.3 % (57/71)	69.0 % (40/58)	0.26908
Dafiro HCT	13.4 % (28/209)	11.3 % (9/80)	12.7 % (9/71)	17.2 % (10/58)	0.58029
Other	10.0 % (21/209)	10.0 % (8/80)	7.0 % (5/71)	13.8 % (8/58)	0.44709
Aliskiren					
Rasilez	100.0 % (18/18)	100.0 % (8/8)	100.0 % (7/7)	100.0 % (3/3)	
Other	0.0 % (0/18)	0.0 % (0/8)	0.0 % (0/7)	0.0 % (0/3)	
Hydrochlorothiazide					
Esidrix	4.3 % (22/511)	6.3 % (13/206)	2.4 % (4/165)	3.6 % (5/140)	0.16440
Other	95.7 % (489/511)	93.7 % (193/206)	97.6 % (161/165)	96.4 % (135/140)	0.16440
Aliskiren / Hydrochlorothiazide					
Rasilez HCT	87.5 % (7/8)	50.0 % (1/2)	100.0 % (4/4)	100.0 % (2/2)	0.18009
Other	12.5 % (1/8)	50.0 % (1/2)	0.0 % (0/4)	0.0 % (0/2)	0.18009
Valsartan / Amlodipine					
Exforge	86.6 % (84/97)	81.6 % (31/38)	90.0 % (36/40)	89.5 % (17/19)	0.50685
Dafiro	10.3 % (10/97)	13.2 % (5/38)	10.0 % (4/40)	5.3 % (1/19)	0.65023
Other	3.1 % (3/97)	5.3 % (2/38)	0.0 % (0/40)	5.3 % (1/19)	0.33749

Table 9-76. *Hypoglycemic events in the SBP treatment groups at 12-month follow-up.*

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
No. of patients with FU data	6666 (100.0 %)	2632 (39.5 %)	2311 (34.7 %)	1723 (25.8 %)	
Hypoglycemic events since last FU					
Without specific symptoms	0.2 % (10/6456)	0.1 % (3/2570)	0.3 % (7/2240)	0.0 % (0/1646)	0.04090
No. of events	2.30 ± 1.89, n=10	1.67 ± 0.58, n=3	2.57 ± 2.23, n=7	, n=0	0.90324[U]
Symptomatic, but controllable without external help	0.1 % (9/6533)	0.0 % (1/2588)	0.1 % (3/2271)	0.3 % (5/1674)	0.08189
No. of events	2.00 ± 1.32, n=9	1.00, n=1	3.33 ± 1.53, n=3	1.40 ± 0.55, n=5	0.07900
External help needed	0.0 % (0/6533)	0.0 % (0/2587)	0.0 % (0/2271)	0.0 % (0/1675)	
No. of events	, n=0	, n=0	, n=0	, n=0	
Symptomatic with medical help	0.0 % (1/6544)	0.0 % (0/2590)	0.0 % (0/2275)	0.1 % (1/1679)	0.23480
No. of events	1.00, n=1	, n=0	, n=0	1.00, n=1	
Hospitalization required	0.0 % (2/6547)	0.0 % (0/2590)	0.0 % (0/2278)	0.1 % (2/1679)	0.05501
No. of events	1.00 ± 0.00, n=2	, n=0	, n=0	1.00 ± 0.00, n=2	

Therapeutic patterns at 24 months follow-up

Table 9-77 shows anti-diabetic therapy in the in the SBP treatment groups at 24-month follow-up (i.e. Metformin; Sulfonylurea drugs; Glucosidase inhibitors; Glinide; Glitazone; DPP-4 inhibitors; GLP-1 analogs; SGTL-2 inhibitors; Total number of antidiabetics; Insulin; Novartis drugs).

Table 9-78 shows anti-hypertensive therapy in the in the SBP treatment groups at 24-month follow-up (i.e. ACE inhibitors; ARB; Direct renin inhibitor; Beta-blocker; Calcium channel blocker; Diuretic drugs; Total number of antihypertensive drugs; Fixed-dose combinations; Novartis drugs).

Table 9-79 shows hypoglycemic events in the in the SBP treatment groups at 24-month follow-up (i.e. Number of events; Type of events; Help needed).

Table 9-77. *Anti-diabetic therapy in the SBP treatment groups at 24-month follow-up.*

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
No. of patients with FU data	4116 (100.0 %)	1636 (39.7 %)	1427 (34.7 %)	1053 (25.6 %)	
Metformin, dosage [mg/day]	1741.48 ± 505.18, n=3276	1701.63 ± 518.06, n=1329	1790.69 ± 476.54, n=1149	1736.98 ± 517.88, n=798	0.00003
Sulfonylurea drugs	18.1 % (744/4116)	16.6 % (271/1636)	18.2 % (260/1427)	20.2 % (213/1053)	0.05405
Sulfonylurea drugs, dosage [mg/day]	3.18 ± 1.86, n=744	3.15 ± 1.92, n=271	3.14 ± 1.66, n=260	3.26 ± 2.01, n=213	0.68385
Substance					
Carbutamide	0.0 % (0/744)	0.0 % (0/271)	0.0 % (0/260)	0.0 % (0/213)	
Tolbutamide	0.0 % (0/744)	0.0 % (0/271)	0.0 % (0/260)	0.0 % (0/213)	
Glibenclamide	19.9 % (148/744)	23.2 % (63/271)	16.9 % (44/260)	19.2 % (41/213)	0.18196
Glibornuride	0.0 % (0/744)	0.0 % (0/271)	0.0 % (0/260)	0.0 % (0/213)	
Gliclazide	0.0 % (0/744)	0.0 % (0/271)	0.0 % (0/260)	0.0 % (0/213)	
Glipizide	0.0 % (0/744)	0.0 % (0/271)	0.0 % (0/260)	0.0 % (0/213)	
Gliquidone	0.4 % (3/744)	0.4 % (1/271)	0.8 % (2/260)	0.0 % (0/213)	0.41947
Glisoxepide	0.0 % (0/744)	0.0 % (0/271)	0.0 % (0/260)	0.0 % (0/213)	
Glycodiazine	0.3 % (2/744)	0.4 % (1/271)	0.4 % (1/260)	0.0 % (0/213)	0.66844
Glimepiride	79.0 % (588/744)	75.6 % (205/271)	81.9 % (213/260)	79.8 % (170/213)	0.19545
Other	0.4 % (3/744)	0.4 % (1/271)	0.0 % (0/260)	0.9 % (2/213)	0.27488
Glucosidase inhibitors	1.2 % (49/4116)	1.3 % (21/1636)	1.2 % (17/1427)	1.0 % (11/1053)	0.85596
Glucosidase inhibitors, dosage [mg/day]	121.12 ± 61.50, n=49	110.71 ± 43.54, n=21	112.35 ± 53.33, n=17	154.55 ± 90.70, n=11	0.36018
Substance					
Acarbose	87.8 % (43/49)	81.0 % (17/21)	88.2 % (15/17)	100.0 % (11/11)	0.29480
Miglitol	10.2 % (5/49)	14.3 % (3/21)	11.8 % (2/17)	0.0 % (0/11)	0.43236
Other	2.0 % (1/49)	4.8 % (1/21)	0.0 % (0/17)	0.0 % (0/11)	0.50634
Glinide	3.6 % (149/4116)	3.0 % (49/1636)	3.4 % (49/1427)	4.8 % (51/1053)	0.03898
Glinide, dosage [mg/day]	8.54 ± 36.66, n=149	13.16 ± 53.30, n=49	3.17 ± 2.11, n=49	9.25 ± 34.59, n=51	0.12581
Substance					
Nateglinide	2.7 % (4/149)	4.1 % (2/49)	0.0 % (0/49)	3.9 % (2/51)	0.36485
Repaglinide	94.6 % (141/149)	95.9 % (47/49)	95.9 % (47/49)	92.2 % (47/51)	0.62685
Other	2.7 % (4/149)	0.0 % (0/49)	4.1 % (2/49)	3.9 % (2/51)	0.36485
Glitazone	0.7 % (28/4116)	0.6 % (10/1636)	1.0 % (14/1427)	0.4 % (4/1053)	0.17970
Glitazone, dosage [mg/day]	38.79 ± 21.65, n=28	38.50 ± 24.04, n=10	37.50 ± 12.82, n=14	44.00 ± 41.56, n=4	0.86190

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
Substance					
Pioglitazon	82.1 % (23/28)	80.0 % (8/10)	100.0 % (14/14)	25.0 % (1/4)	0.00250
Other	17.9 % (5/28)	20.0 % (2/10)	0.0 % (0/14)	75.0 % (3/4)	0.00250
DPP-4 inhibitors	59.7 % (2457/4116)	57.6 % (943/1636)	61.5 % (878/1427)	60.4 % (636/1053)	0.07892
DPP-4 inhibitors, dosage [mg/day]	83.49 ± 34.30, n=2457	85.81 ± 37.57, n=943	81.28 ± 33.07, n=878	83.09 ± 30.50, n=636	0.35137
Substance					
Sitagliptin	44.7 % (1098/2457)	46.8 % (441/943)	41.9 % (368/878)	45.4 % (289/636)	0.10399
Vildagliptin	47.3 % (1162/2457)	46.8 % (441/943)	48.2 % (423/878)	46.9 % (298/636)	0.80664
Linagliptin	0.0 % (0/2457)	0.0 % (0/943)	0.0 % (0/878)	0.0 % (0/636)	
Saxagliptin	7.5 % (184/2457)	6.0 % (57/943)	9.7 % (85/878)	6.6 % (42/636)	0.00803
Other	0.5 % (13/2457)	0.4 % (4/943)	0.2 % (2/878)	1.1 % (7/636)	0.05904
GLP-1 analogs/mimetics	5.1 % (211/4116)	4.8 % (79/1636)	5.5 % (79/1427)	5.0 % (53/1053)	0.66728
GLP-1 analogs/mimetics, dosage [mg/day]	7.73 ± 15.46, n=211	5.91 ± 8.33, n=79	6.90 ± 17.41, n=79	11.69 ± 19.60, n=53	0.02875
Substance					
Exenatide	41.7 % (88/211)	30.4 % (24/79)	48.1 % (38/79)	49.1 % (26/53)	0.03552
Liraglutide	57.3 % (121/211)	67.1 % (53/79)	51.9 % (41/79)	50.9 % (27/53)	0.08577
Other	0.9 % (2/211)	2.5 % (2/79)	0.0 % (0/79)	0.0 % (0/53)	0.18510
SGTL-2 inhibitors	2.9 % (120/4116)	2.5 % (41/1636)	3.5 % (50/1427)	2.8 % (29/1053)	0.24526
SGTL-2 inhibitors, dosage [mg/day]	14.55 ± 19.87, n=119	12.50 ± 14.41, n=40	16.90 ± 24.78, n=50	13.31 ± 16.80, n=29	0.98580
Substance					
Dapagliflozin	89.2 % (107/120)	90.2 % (37/41)	84.0 % (42/50)	96.6 % (28/29)	0.21563
Other	10.8 % (13/120)	9.8 % (4/41)	16.0 % (8/50)	3.4 % (1/29)	0.21563
Insulin(rapid-acting or long-acting or Pre-mixed)	19.9 % (821/4116)	16.8 % (275/1636)	24.4 % (348/1427)	18.8 % (198/1053)	<.00001
Rapid-acting insulin	7.6 % (313/4116)	6.1 % (99/1636)	8.9 % (127/1427)	8.3 % (87/1053)	0.00794
Human insulin	40.6 % (127/313)	42.4 % (42/99)	36.2 % (46/127)	44.8 % (39/87)	0.40826
Analogues	59.4 % (186/313)	57.6 % (57/99)	63.8 % (81/127)	55.2 % (48/87)	0.40826
Syringe	2.9 % (9/313)	2.0 % (2/99)	2.4 % (3/127)	4.6 % (4/87)	0.52123
Pen	97.1 % (304/313)	98.0 % (97/99)	97.6 % (124/127)	95.4 % (83/87)	0.52123
Pump	0.0 % (0/313)	0.0 % (0/99)	0.0 % (0/127)	0.0 % (0/87)	

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
Other	0.0 % (0/313)	0.0 % (0/99)	0.0 % (0/127)	0.0 % (0/87)	
U-40	15.8 % (49/311)	17.2 % (17/99)	15.9 % (20/126)	14.0 % (12/86)	0.83473
U-100	84.2 % (262/311)	82.8 % (82/99)	84.1 % (106/126)	86.0 % (74/86)	0.83473
1x insulin/day	8.9 % (28/313)	11.1 % (11/99)	7.9 % (10/127)	8.0 % (7/87)	0.65855
2x insulin/day	13.1 % (41/313)	12.1 % (12/99)	15.0 % (19/127)	11.5 % (10/87)	0.71655
3x insulin/day	76.0 % (238/313)	75.8 % (75/99)	73.2 % (93/127)	80.5 % (70/87)	0.47518
4x insulin/day	1.9 % (6/313)	1.0 % (1/99)	3.9 % (5/127)	0.0 % (0/87)	0.08674
Long-acting insulin	18.5 % (761/4116)	15.6 % (256/1636)	22.8 % (326/1427)	17.0 % (179/1053)	<.00001
Human insulin	30.6 % (233/761)	33.2 % (85/256)	26.4 % (86/326)	34.6 % (62/179)	0.08535
Analogues	69.4 % (528/761)	66.8 % (171/256)	73.6 % (240/326)	65.4 % (117/179)	0.08535
Syringe	4.9 % (37/761)	7.0 % (18/256)	2.8 % (9/326)	5.6 % (10/179)	0.05184
Pen	94.6 % (720/761)	92.6 % (237/256)	96.9 % (316/326)	93.3 % (167/179)	0.04667
Pump	0.1 % (1/761)	0.0 % (0/256)	0.0 % (0/326)	0.6 % (1/179)	0.19635
Other	0.4 % (3/761)	0.4 % (1/256)	0.3 % (1/326)	0.6 % (1/179)	0.91080
U-40	13.3 % (101/759)	16.4 % (42/256)	8.9 % (29/325)	16.9 % (30/178)	0.00871
U-100	86.7 % (658/759)	83.6 % (214/256)	91.1 % (296/325)	83.1 % (148/178)	0.00871
1x insulin/day	87.0 % (662/761)	87.1 % (223/256)	86.2 % (281/326)	88.3 % (158/179)	0.80128
2x insulin/day	12.2 % (93/761)	12.1 % (31/256)	12.6 % (41/326)	11.7 % (21/179)	0.96014
3x insulin/day	0.7 % (5/761)	0.4 % (1/256)	1.2 % (4/326)	0.0 % (0/179)	0.21387
4x insulin/day	0.1 % (1/761)	0.4 % (1/256)	0.0 % (0/326)	0.0 % (0/179)	0.37246
Pre-mixed insulin	2.3 % (96/4116)	1.9 % (31/1636)	2.7 % (38/1427)	2.6 % (27/1053)	0.31546
Human insulin	69.8 % (67/96)	83.9 % (26/31)	65.8 % (25/38)	59.3 % (16/27)	0.09906
Analogues	30.2 % (29/96)	16.1 % (5/31)	34.2 % (13/38)	40.7 % (11/27)	0.09906
Syringe	3.1 % (3/96)	6.5 % (2/31)	2.6 % (1/38)	0.0 % (0/27)	0.36155
Pen	96.9 % (93/96)	93.5 % (29/31)	97.4 % (37/38)	100.0 % (27/27)	0.36155
Pump	0.0 % (0/96)	0.0 % (0/31)	0.0 % (0/38)	0.0 % (0/27)	
Other	0.0 % (0/96)	0.0 % (0/31)	0.0 % (0/38)	0.0 % (0/27)	

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
U-40	12.8 % (12/94)	22.6 % (7/31)	2.6 % (1/38)	16.0 % (4/25)	0.04034
U-100	87.2 % (82/94)	77.4 % (24/31)	97.4 % (37/38)	84.0 % (21/25)	0.04034
1x insulin/day	10.4 % (10/96)	6.5 % (2/31)	5.3 % (2/38)	22.2 % (6/27)	0.05971
2x insulin/day	79.2 % (76/96)	80.6 % (25/31)	78.9 % (30/38)	77.8 % (21/27)	0.96379
3x insulin/day	9.4 % (9/96)	12.9 % (4/31)	13.2 % (5/38)	0.0 % (0/27)	0.14318
4x insulin/day	1.0 % (1/96)	0.0 % (0/31)	2.6 % (1/38)	0.0 % (0/27)	0.46246
Fixed-dose combination metformin / DPP-4 inhibitor	77.5 % (1557/2008)	77.5 % (611/788)	76.0 % (549/722)	79.7 % (397/498)	0.31793
Novartis drugs					
Vildagliptin / Metformin					
Eucreas	92.5 % (723/782)	93.1 % (283/304)	92.0 % (263/286)	92.2 % (177/192)	0.86163
Icandra	7.5 % (59/782)	6.9 % (21/304)	8.0 % (23/286)	7.8 % (15/192)	0.86163
Vildagliptin					
Galvus	87.9 % (333/379)	86.9 % (119/137)	86.8 % (118/136)	90.6 % (96/106)	0.60381
Jalra	12.1 % (46/379)	13.1 % (18/137)	13.2 % (18/136)	9.4 % (10/106)	0.60381
Nateglinide					
STARLIX	100.0 % (4/4)	100.0 % (2/2)		100.0 % (2/2)	
Other	0.0 % (0/4)	0.0 % (0/2)		0.0 % (0/2)	

Table 9-78. *Anti-hypertensive therapy in the SBP treatment groups at 24-month follow-up.*

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
No. of patients with FU data	4116 (100.0 %)	1636 (39.7 %)	1427 (34.7 %)	1053 (25.6 %)	
ACE inhibitors	52.8 % (2173/4116)	51.1 % (836/1636)	53.4 % (762/1427)	54.6 % (575/1053)	0.17554
ACE inhibitors, dosage [mg/day]	10.0 (5.0, 10.0)	10.0 (5.0, 10.0)	10.0 (5.0, 10.0)	10.0 (5.0, 10.0)	0.43549
Substance					
Captopril	2.5 % (54/2173)	2.8 % (23/836)	2.2 % (17/762)	2.4 % (14/575)	0.79718
Enalapril	20.0 % (434/2173)	22.4 % (187/836)	18.4 % (140/762)	18.6 % (107/575)	0.08665
Lisinopril	10.6 % (230/2173)	9.9 % (83/836)	11.2 % (85/762)	10.8 % (62/575)	0.71670
Ramipril	64.0 % (1391/2173)	62.2 % (520/836)	65.2 % (497/762)	65.0 % (374/575)	0.37889
Trandolapril	0.2 % (4/2173)	0.2 % (2/836)	0.1 % (1/762)	0.2 % (1/575)	0.87921
Other	2.8 % (60/2173)	2.5 % (21/836)	2.9 % (22/762)	3.0 % (17/575)	0.85208
Angiotensin receptor blocker (ARB)	30.0 % (1233/4116)	29.2 % (477/1636)	30.6 % (437/1427)	30.3 % (319/1053)	0.65081
ARB, dosage [mg/day]	80.0 (20.0, 160.0)	80.0 (32.0, 160.0)	80.0 (20.0, 160.0)	80.0 (20.0, 160.0)	0.48575
Substance					
Candesartan	24.0 % (296/1233)	23.5 % (112/477)	25.2 % (110/437)	23.2 % (74/319)	0.77411
Irbesartan	5.0 % (62/1233)	5.9 % (28/477)	3.4 % (15/437)	6.0 % (19/319)	0.16422
Losartan	7.2 % (89/1233)	5.5 % (26/477)	8.0 % (35/437)	8.8 % (28/319)	0.15022
Valsartan	40.2 % (496/1233)	41.7 % (199/477)	39.8 % (174/437)	38.6 % (123/319)	0.65647
Other	23.5 % (290/1233)	23.5 % (112/477)	23.6 % (103/437)	23.5 % (75/319)	0.99948
Direct renin inhibitor	0.3 % (12/4116)	0.4 % (6/1636)	0.4 % (5/1427)	0.1 % (1/1053)	0.38906
Direct renin inhibitor, dosage [mg/day]	225.0 (150.0, 300.0)	150.0 (150.0, 300.0)	300.0 (300.0, 300.0)	150.0 (150.0, 150.0)	0.21309
Beta-blocker	49.8 % (2048/4116)	49.0 % (802/1636)	51.5 % (735/1427)	48.5 % (511/1053)	0.25447
Beta-blocker, dosage [mg/day]	25.0 (5.0, 95.0)	37.8 (5.0, 95.0)	47.5 (5.0, 100.0)	10.0 (5.0, 95.0)	0.00218
Substance					
Metoprolol	45.9 % (941/2048)	47.5 % (381/802)	48.3 % (355/735)	40.1 % (205/511)	0.00903
Bisoprolol	41.0 % (840/2048)	40.4 % (324/802)	38.6 % (284/735)	45.4 % (232/511)	0.05224
Nebivolol	5.6 % (115/2048)	4.7 % (38/802)	5.9 % (43/735)	6.7 % (34/511)	0.31976

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
Carvedilol	4.2 % (85/2048)	4.1 % (33/802)	3.9 % (29/735)	4.5 % (23/511)	0.88783
Other	3.3 % (67/2048)	3.2 % (26/802)	3.3 % (24/735)	3.3 % (17/511)	0.99638
Calcium channel blocker	30.6 % (1258/4116)	28.1 % (460/1636)	31.1 % (444/1427)	33.6 % (354/1053)	0.00889
Calcium channel blocker, dosage [mg/day]	10.0 (5.0, 10.0)	10.0 (5.0, 10.0)	10.0 (5.0, 10.0)	10.0 (5.0, 10.0)	0.88898
Substance					
Amlodipine	76.1 % (957/1258)	77.0 % (354/460)	75.9 % (337/444)	75.1 % (266/354)	0.82971
Nifedipine	1.8 % (23/1258)	1.1 % (5/460)	2.5 % (11/444)	2.0 % (7/354)	0.28724
Nisoldipine	0.0 % (0/1258)	0.0 % (0/460)	0.0 % (0/444)	0.0 % (0/354)	
Nimodipine	0.1 % (1/1258)	0.2 % (1/460)	0.0 % (0/444)	0.0 % (0/354)	0.41976
Diltiazem	0.7 % (9/1258)	0.4 % (2/460)	0.0 % (0/444)	2.0 % (7/354)	0.00296
Verapamil	2.6 % (33/1258)	2.0 % (9/460)	2.9 % (13/444)	3.1 % (11/354)	0.52555
Gallopamil	0.0 % (0/1258)	0.0 % (0/460)	0.0 % (0/444)	0.0 % (0/354)	
Felodipine	2.9 % (36/1258)	3.0 % (14/460)	3.4 % (15/444)	2.0 % (7/354)	0.47785
Nitrendipine	4.3 % (54/1258)	4.6 % (21/460)	5.6 % (25/444)	2.3 % (8/354)	0.06147
Lercanidipine	10.2 % (128/1258)	9.8 % (45/460)	8.3 % (37/444)	13.0 % (46/354)	0.09054
Nilvadipine	0.1 % (1/1258)	0.2 % (1/460)	0.0 % (0/444)	0.0 % (0/354)	0.41976
Manidipine	0.1 % (1/1258)	0.2 % (1/460)	0.0 % (0/444)	0.0 % (0/354)	0.41976
Isradipine	0.1 % (1/1258)	0.2 % (1/460)	0.0 % (0/444)	0.0 % (0/354)	0.41976
Other	1.1 % (14/1258)	1.3 % (6/460)	1.4 % (6/444)	0.6 % (2/354)	0.50958
Diuretic drugs	45.4 % (1867/4116)	43.4 % (710/1636)	45.6 % (651/1427)	48.1 % (506/1053)	0.05901
Diuretic drugs, dosage [mg/day]	20.0 (12.5, 25.0)	22.5 (12.5, 25.0)	20.0 (12.5, 25.0)	12.5 (12.5, 25.0)	0.05942
Substance					
Furosemide	7.7 % (143/1867)	8.5 % (60/710)	7.2 % (47/651)	7.1 % (36/506)	0.60083
Torasemide	21.9 % (408/1867)	19.9 % (141/710)	22.4 % (146/651)	23.9 % (121/506)	0.21917
Bumetanide	0.1 % (1/1867)	0.0 % (0/710)	0.2 % (1/651)	0.0 % (0/506)	0.39280
Etacrynic acid	0.1 % (1/1867)	0.0 % (0/710)	0.2 % (1/651)	0.0 % (0/506)	0.39280
Piretanide	1.4 % (27/1867)	2.1 % (15/710)	1.5 % (10/651)	0.4 % (2/506)	0.04571
Hydrochlorothiazide	71.5 % (1334/1867)	73.1 % (519/710)	70.4 % (458/651)	70.6 % (357/506)	0.46550
Clopamid	0.3 % (5/1867)	0.4 % (3/710)	0.0 % (0/651)	0.4 % (2/506)	0.26025
Other	8.4 % (156/1867)	7.3 % (52/710)	9.7 % (63/651)	8.1 % (41/506)	0.28444

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
Other anti-hypertensive therapy	11.0 % (454/4116)	10.0 % (163/1636)	11.1 % (158/1427)	12.6 % (133/1053)	0.09787
Fixed-dose combinations					
Fixed-dose combination ARB/calcium channel blocker/diuretic	72.6 % (276/380)	73.2 % (104/142)	68.1 % (92/135)	77.7 % (80/103)	0.25835
Fixed-dose combination ACE inhibitor/diuretic	50.3 % (467/929)	53.0 % (186/351)	50.0 % (163/326)	46.8 % (118/252)	0.32539
Fixed-dose combination ARB/diuretic	65.3 % (328/502)	62.6 % (117/187)	62.7 % (116/185)	73.1 % (95/130)	0.09831
Fixed-dose combination ARB/calcium channel blocker	41.1 % (113/275)	45.2 % (47/104)	40.9 % (45/110)	34.4 % (21/61)	0.39781
Fixed-dose combination ACE inhibitor/calcium channel blocker	17.0 % (104/611)	15.2 % (32/210)	17.2 % (36/209)	18.8 % (36/192)	0.64238
Fixed-dose combination direct renin inhibitor/diuretic	44.4 % (4/9)	60.0 % (3/5)	25.0 % (1/4)		0.29372
Novartis drugs					
Valsartan / Hydrochlorothiazide					
CoDiovan	27.0 % (31/115)	37.5 % (15/40)	20.0 % (9/45)	23.3 % (7/30)	0.16828
Codiovan forte	11.3 % (13/115)	15.0 % (6/40)	8.9 % (4/45)	10.0 % (3/30)	0.65128
Cordinate plus	3.5 % (4/115)	5.0 % (2/40)	4.4 % (2/45)	0.0 % (0/30)	0.47661
Provas	0.9 % (1/115)	0.0 % (0/40)	2.2 % (1/45)	0.0 % (0/30)	0.45630
Provas comp	4.3 % (5/115)	2.5 % (1/40)	8.9 % (4/45)	0.0 % (0/30)	0.14062
Provas maxx	1.7 % (2/115)	2.5 % (1/40)	0.0 % (0/45)	3.3 % (1/30)	0.50204
Other	51.3 % (59/115)	37.5 % (15/40)	55.6 % (25/45)	63.3 % (19/30)	0.07753
Valsartan					
Cordinate	2.0 % (3/151)	1.5 % (1/65)	0.0 % (0/49)	5.4 % (2/37)	0.19388
Diovan	27.8 % (42/151)	30.8 % (20/65)	28.6 % (14/49)	21.6 % (8/37)	0.60551
Provas	7.3 % (11/151)	4.6 % (3/65)	2.0 % (1/49)	18.9 % (7/37)	0.00642
Other	62.9 % (95/151)	63.1 % (41/65)	69.4 % (34/49)	54.1 % (20/37)	0.34547
Valsartan / Amlodipine / Hydrochlorothiazide					
Exforge HCT	73.6 % (103/140)	74.1 % (43/58)	79.1 % (34/43)	66.7 % (26/39)	0.44166
Dafiro HCT	15.7 % (22/140)	13.8 % (8/58)	14.0 % (6/43)	20.5 % (8/39)	0.62491
Other	10.7 % (15/140)	12.1 % (7/58)	7.0 % (3/43)	12.8 % (5/39)	0.63128
Aliskiren					
Rasilez	100.0 % (8/8)	100.0 % (3/3)	100.0 % (4/4)	100.0 % (1/1)	
Other	0.0 % (0/8)	0.0 % (0/3)	0.0 % (0/4)	0.0 % (0/1)	
Hydrochlorothiazide					

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
Esidrix	4.6 % (16/346)	6.7 % (10/149)	1.8 % (2/113)	4.8 % (4/84)	0.16841
Other	95.4 % (330/346)	93.3 % (139/149)	98.2 % (111/113)	95.2 % (80/84)	0.16841
Aliskiren / Hydrochlorothiazide					
Rasilez HCT	75.0 % (3/4)	66.7 % (2/3)	100.0 % (1/1)		0.50499
Other	25.0 % (1/4)	33.3 % (1/3)	0.0 % (0/1)		0.50499
Valsartan / Amlodipine					
Exforge	80.6 % (58/72)	74.2 % (23/31)	86.2 % (25/29)	83.3 % (10/12)	0.48397
Dafiro	13.9 % (10/72)	16.1 % (5/31)	13.8 % (4/29)	8.3 % (1/12)	0.80253
Other	5.6 % (4/72)	9.7 % (3/31)	0.0 % (0/29)	8.3 % (1/12)	0.23620

Table 9-79. *Hypoglycemic events in the SBP treatment groups at 24-month follow-up.*

	TOTAL	SBP <= 130	SBP >130 - <= 135	SBP >135 - <= 140	P-value
No. of patients with FU data	4116 (100.0 %)	1636 (39.7 %)	1427 (34.7 %)	1053 (25.6 %)	
Hypoglycemic events since last FU					
Without specific symptoms	0.3 % (12/4025)	0.2 % (4/1610)	0.4 % (5/1391)	0.3 % (3/1024)	0.85616
No. of events	1.92 ± 1.44, n=12	1.50 ± 0.58, n=4	2.80 ± 1.92, n=5	1.00 ± 0.00, n=3	0.09231
Symptomatic, but controllable without external help	0.2 % (10/4059)	0.1 % (2/1616)	0.5 % (7/1413)	0.1 % (1/1030)	0.06431
No. of events	4.20 ± 3.82, n=10	8.50 ± 4.95, n=2	3.43 ± 3.05, n=7	1.00, n=1	0.09533
External help needed	0.0 % (0/4065)	0.0 % (0/1619)	0.0 % (0/1416)	0.0 % (0/1030)	
No. of events	, n=0	, n=0	, n=0	, n=0	
Symptomatic with medical help	0.0 % (0/4065)	0.0 % (0/1619)	0.0 % (0/1416)	0.0 % (0/1030)	
No. of events	, n=0	, n=0	, n=0	, n=0	
Hospitalization required	0.0 % (1/4065)	0.1 % (1/1619)	0.0 % (0/1416)	0.0 % (0/1030)	0.46973
No. of events	1.00, n=1	1.00, n=1	, n=0	, n=0	

9.5 Other Subgroup Analyses

Descriptive statistical reports of subgroups (Female vs. Male; Age > 75 years vs. Age ≤ 75 years) are given in Appendix 7.

9.6 Adverse Events and Adverse Reactions

Line listings of adverse events (see section 8.9.4 for AE definition and structure of line listings) are given in Appendix 3.

10 Discussion

10.1 Key Results

Overall, 8,568 hypertensive T2DM patients from 511 active sites were enrolled at baseline. Among those 2,991 patients (34.9%) were initially treated with non-incretin-based medication and 5,577 patients with incretin-based medication. Among patients with incretin-based therapy, 3,487 (62.5%) patients were treated with vildagliptin and 2,090 (37.5%) with other incretin-based medication. Patients were followed-up at 6, 12, and 24 months after baseline visit. Numbers of documented follow-up visits at 24 months were particularly low (only about 50% of all enrolled patients had documented follow-up visits at 24 months), since not all patients had a 24-month follow-up visit (due to the fact that on 1st July 2014, the antidiabetics Galvus®/Eucreas® were withdrawn from the market, and thus, the registry and the documentation of follow-up visits was prematurely concluded in December 2014).

For the evaluation of individualized treatment targets and their achievement patients were categorized into three groups based on treatment goals regarding (1) initial HbA1c treatment goals (≤ 6.5% [strict] / >6.5 – 7.0% [medium] / >7.0 – ≤ 7.5% [loose]) and on (2) initial SBP treatment goals (≤ 130 mmHg [strict] / >130 – 135 mmHg [medium] / >135 – - ≤ 140 mmHg [loose]).

Multivariate analyses regarding factors contributing to the assignment of patients into the loose target groups for both HbA1c and SBP revealed that loose HbA1c targets were weakly correlated with age, gender, fasting blood glucose, SBP, heart failure and peripheral arterial disease with the HbA1c value at baseline as the strongest predictor. Similarly, loose SBP targets were weakly correlated with age, fasting blood glucose, heart failure, peripheral arterial disease, and neuropathy with the SBP value at baseline as the strongest predictor.

Analyses of the relationship between patients with distinct HbA1c and SBP treatment goals showed that about 70% of patients with strict HbA1c treatment targets also had strict SBP treatment goals. The same could be observed for cross comparison of the medium and loose treatment groups (about 52% and 61% of patients in the respective HbA1c target groups coincided with the corresponding SBP target groups).

Target achievement rates were calculated for 6-, 12-, and 24-month follow-ups. Regarding the HbA1c treatment targets, at least about half of the patients met their pre-defined treatment

targets (strict target: 45.8% at 6M-FU, 46.2% at 12M-FU, 46% at 24M-FU; medium target: 51.4% at 6M-FU, 56.8% at 12M-FU, 61.5% at 24M-FU; loose target: 53.3% at 6M-FU, 59.4% at 12M-FU, 64.5% at 24M-FU). Regarding the SBP treatment targets, more than 50% of the patients met their pre-defined treatment targets (strict target: 51.4% at 6M-FU, 50.8% at 12M-FU, 50.3% at 24M-FU; medium target: 54.5% at 6M-FU, 56.4% at 12M-FU, 60.6% at 24M-FU; loose target: 65.0% at 6M-FU, 67.3% at 12M-FU, 72.4% at 24M-FU).

10.2 Limitations

This investigation was subject to some limitations. Indeed, the patients analyzed in the present study were comorbid for T2DM and hypertension and were often administered combined therapy regimens, which could have confounded data interpretation. However, since DIALOGUE is an observational study conducted in real clinical settings with physician-selected therapy, our results are highly representative of individualized treatment regimens currently employed for patients with T2DM and hypertension. In addition, it has been suggested that registry data can be less complete when compared to information collected in randomized clinical trials. However, in this regard, three strategies were implemented to assure information quality, including front-end checks upon data entry, use of a sophisticated quality control program prior to creation of the analytic data set, and random site visits (monitoring).

10.3 Generalizability

In contrast to randomized controlled trials, non-interventional observational studies present data of an unselected patient population within real clinical settings to compare treatment effectiveness in real-world practice. The usually large number of patients enrolled permits results to be generalized to the whole population of patients affected. The advantage of using a disease-based registry, such as DIALOGUE, is that almost all patients are included who meet the disease criteria. Additionally, follow-up periods are usually much longer compared to randomized controlled trials; and thus, especially rare adverse events can be identified. Moreover, useful interventions may derive from large non-interventional studies. Non-interventional studies should be considered as complementary to randomized controlled trials, and can provide more robust evidence when considered together. However, selection bias must be attenuated. Observational studies are particularly liable to bias (systematic error in the design and methods of the study) resulting in incorrect interpretation of study results. In contrast to randomized clinical trials, observational studies cannot control or minimize systematic sources of bias by randomly assigning the subjects to different groups.

To avoid a selection bias, investigators of all participating sites were asked to document patients consecutively to achieve a representative cross-section of hypertensive T2DM patients in Germany. In this case, with an observational study the bias due to patient selection by unknown circumstances may not have been completely prevented, but was small compared to retrospective studies. To ensure the completeness of the data collected and consistent data collection among the different centers standardized case record forms (CRF) were used for data entry. Quality assuring measures were established during data entry: e.g. as a basis for the plausibility checks: range checks or cross checks of variables. Ambiguity through a lack of readability, incompleteness and implausibility was solved by queries. Due to the cross-

sectional design and descriptive nature of the study, causal inference is difficult to make. Therefore, potential confounders were incorporated in the regression models as explanatory risk factors.

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11 Appendices

Appendix 1 Observational Plan and Case Report Form

Appendix 2 Investigator List

Appendix 3 Adverse Events and Adverse Reactions

Appendix 4 List of Publications

Appendix 5 Statistical analyses of treatment groups (Vildagliptin vs. other incretin-based treatment vs. non-incretin-based treatment)

Appendix 6 Statistical analyses of treatment target groups (HbA1c targets; SBP targets)

Appendix 7 Statistical analyses of subgroups (Gender; Age)