Type 2 Diabetes in General Practice in Norway 2005-14: Moderate Improvements in Risk Factor Control but Still Major Gaps in Complication Screening

Type 2 Diabetes Care in General Practice

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Abstract (244/250 words)

Objective: To assess the status of type 2 diabetes care in general practice, changes in the quality of care between 2005 and 2014 and to identify areas of diabetes care requiring improvement.

Research Design and Methods: Two cross-sectional surveys were performed that included patients with type 2 diabetes in selected areas (n=9464 in 2014, n=5463 in 2005). Quality of care was assessed based on key recommendations in national guidelines. Differences in clinical performance between 2005 and 2014 were assessed in regression models adjusting for age, sex, counties and clustering within GP practices.

Results: Treatment targets were achieved in a higher proportion of patients in 2014 compared with 2005; HbA_{1c} ≤7.0% (≤53 mmol/mol) in 62.8% vs. 54.3%, blood pressure ≤135/80 mmHg in 44.9% vs. 36.6% and total cholesterol ≤4.5 mmol/L in 49.9% vs. 33.5% (all adjusted p≤0.001). Screening procedures for microvascular complications:

Less patients had recorded an eye examination (61.0% vs. 71.5%, adjusted p<0.001) wheras more patients underwent monofilament test (25.9% vs. 18.7%, adjusted p<0.001). Testing for albuminuria remained low (30.3%) in 2014. A still high percentage were current smokers, 22.7%.

Conclusions: We found a moderate improvement in risk-factor control for type 2 diabetes patients in general practice during the last decade that are similar to improvements reported in other countries. We report major gaps in the performance of recommended screening procedures to detect microvascular complications. The proportion of daily smokers remains high. We suggest incentives to promote further improvements in diabetes care in Norway.

Good glycemic control and appropriate management of cardiovascular risk factors in patients with type 2 diabetes reduce the risk of vascular complications and mortality (1-9). The Steno-2 trial found an increase in lifespan in high-risk patients with type 2 diabetes with a combined behavioural and pharmacological intervention in a specialist care setting (5). However, in most countries the majority of patients with type 2 diabetes are treated in primary care. The initial 5-year follow-up of the ADDITION-Europe trial of screening detected type 2 diabetes patients in general practice found improved risk factor levels and a trend towards a reduced rate of cardiovascular events, microvascular complications and death in the multifactorial treatment group compared with routine care (10; 11). A Swedish observational study with 13 000 patients with type 2 diabetes from general practice in 2012 reported that fatal and non-fatal CVD decreased from 23.6% to 6.0% when they compared patients achieving a decrease

versus an increase in HbA1c, blood pressure and lipids (4). It has also been shown that early detection of complications by systematic screening and intervention prevents or delays the development of target organ disease (12; 13).

Risk factor control and screening for early complications can only be closely monitored in countries with nationwide and comprehensive diabetes registries such as Sweden and Scotland (14; 15). Other countries must perform cross-sectional surveys to assess status and time trends in diabetes care (16-19). In Norway, the quality of type 2 diabetes care has been assessed through repeated cross-sectional surveys (ROSA studies) since 1995. The previous survey, ROSA 3, was performed in 2005 and showed substantial improvements in glycemic-, blood pressure- and lipid control between 1995 and 2005 (20; 21).

A new assessment of the quality of diabetes care was important for several reasons. Firstly, several new glucose lowering agents have been approved since 2005, and antihyperglycemic drug expenditure has increased world wide (22; 23). Secondly, during the last decade several large studies comparing different treatment targets for diabetes have failed to show additional benefit from extremely intensive treatment targets (24-26). As a result of these studies modern diabetes guidelines emphasize the importance of individual treatment targets that may influence the overall quality of care (27-29). Finally, Norway offers government funded health care services to all inhabitants and these services are expected to provide high quality diabetes care. We therefore designed a large cross-sectional survey in 2014, the ROSA 4 study, with the objective of assessing the current status of type 2 diabetes care in general practice, changes in the quality of care between 2005 and 2014, and identifying areas of care requiring improvement.

Research Design and Methods

ROSA 4 is a population-based cross-sectional survey designed to assess the quality of care of patients with type 2 diabetes in general practice in Norway in 2014. We included diabetes patients living in urban and rural areas in three out of four health regions covering more than 50% of the population in Norway. GPs in these areas were invited to participate, and 77 practices (73% of the invited) with 282 GP's (77% of the invited) agreed (Flowchart, Supplemental Figure S1). Data were collected from the electronic patient records from all the GPs within a practice by research nurses.

All adults (≥18 years) with a diagnosis of diabetes between 2012-2014 were identified using customized software that also captured predefined data from the electronic patient records. The records were examined manually by research nurses to verify electronically registered data and to collect data not suitable for electronic capture. Data capture was performed January 2015 – April 2016.

The following variables were registered in the survey: patient characteristics (age, sex, ethnicity, diabetes duration, height and weight, smoking status); processes of care (documentation of HbA1c, blood pressure, lipids, creatinine/estimated glomerulofiltration rate (eGFR), height and weight, smoking habits, eye examination, albuminuria, monofilament test); medication (antihyperglycemic-, antihypertensive-, antithrombotic- and lipidlowering therapy extracted from the GP's electronic prescription files); intermediate outcomes (HbA1c, blood pressure, cholesterol, LDL, creatinine/eGFR); and vascular complications (retinopathy, nephropathy (albuminuria, eGFR <60 ml/min/1.73 m^2), neuropathy (pathological 10-g monofilament test), foot ulcer, lower limb amputation,

coronary heart disease (angina, myocardial infarction, percutaneous coronary intervention/coronary artery bypass surgery), stroke (excluding transient ishemic attacks), atrial fibrillation, percutaneous transluminal angioplasty/arterial surgery. In the present study we included the last registered value in 2014 for most variables, except for eye examination, creatinine/eGFR and lipids (last registered 2012-2014), and smoking habits (last registered 2010-2014) (Supplemental Table S1). Medication was extracted from the GP's electronical prescriptions the last 15 months, October 1st 2013 to December 31st 2014.

ROSA 4 was approved by the Regional Ethical Committee in Norway.

Of the 11 428 patients in the electronic patient records with diabetes, 10 248 had type 2 diabetes. Patients who did not have their main follow-up in general practice (residential patients in nursing homes (n=63), patients attending a specialist clinic >1 time/year (n=421), patients with a diabetes duration of less than 6 months and patients that had died or moved from the practice area during 2014 (n=300)), in total n=784 (8%) were excluded from the analysis, leaving 9464 type 2 diabetes patients for statistical analysis (Supplemental Figure S1).

The ROSA 3 survey in 2005 used the same inclusion and exclusion criteria and methods of data extraction as ROSA 4 (20; 30) and consisted of a sample of 5463 type 2 diabetes patients treated in primary care, from 60 practices and 205 GPs (Supplemental Figure S2). The ROSA 4 and ROSA 3 datasets used the same variable definition for almost all variables, except that the variable stroke excluded transient ischemic attacks (TIA) in 2014, wheras TIA was included in 2005 (Supplemental Table S1).

Quality of care was assessed against predefined review criteria based on key recommendations in the Norwegian 2009-guidelines (31): HbA_{1c} ≤7.0% (53 mmol/mol), intervention threshold blood pressure >140/85 mmHg with treatment target ≤135/80 mmHg, total cholesterol ≤4.5 mmol/L. LDL targets were introduced with revision of the guidelines in 2009 but was not used in the comparison analyses due to missing data in the ROSA 3 survey.

Statistical analyses

We compared 2014 data with 2005 in regression models while controlling for patient age, gender and county of GP practice. We present average adjusted predictions (AAP) with confidence intervals (CI) adjusted for clustering within GP practices. Differences were tested for statistical significance using Wald tests. We did not control for diabetes duration since new patients may have been diagnosed at an earlier stage in the ROSA 4 study due to the introduction of HbA_{1c} >6.5% (48 mmol/mol) as diagnostic criterium. All statistical analyses were performed using STATA/SE 14.0 for Windows, with functions logit, mlogit and regress, and with margins and test postestimation procedures. In consideration of the large sample size and correspondingly high statistical power, we applied a somewhat strict criterium ($p \leq 0.01$) for statistical significance.

In 2014, data were collected from two more counties than in 2005. We therefore performed a sensitivity analysis comparing data only from the three counties included in both ROSA 3 and 4. This analysis gave almost identical results for all variables (data not shown).

Results

Study samples

In 2014, 73% of GP practices agreed to participate compared with 91% in 2005. We included 9464 (2014) and 5463 (2005) patients with type 2 diabetes. Characteristics of the study samples are presented in Supplemental Table S2. There were more urban residents (85.2% vs. 80.4%) and more males (54.6% vs. 50.4%) included in 2014 compared with 2005, and the 2014-patients also had a longer duration of diabetes (median duration 7 years vs. 5 years). The samples were similar with regard to age, ethnicity, BMI, and proportion of current smokers. The proportion of smokers was higher among patients <60 years vs. ≥60 years in both 2014 (29.7% vs. 19.3%) and 2005 (33.8% vs. 20.4%).

Processes of care (Table 1)

HbA_{1c}, blood pressure and cholesterol were measured in most patients (>85%) in both study years, however HbA_{1c} was performed in a lower proportion in 2014 compared with 2005 (86.4% vs. 91.8%, adjusted change -4.4 percentage points, p<0.001). Frequencies of measurement of LDL and creatinine/eGRF were also high in 2014, with 84.4% and 93.2% of patients, respectively. Recording of both height/weight to estimate BMI was low in both study years (44.6% in 2014), whereas registration of smoking habits increased (79.0% vs. 56.0%, adjusted change +24.9 percentage points, p<0.001). Procedures related to screening for microvascular complications differed between 2014 and 2005, with fewer patients undergoing eye examination in 2014 (61.0% vs. 71.5%, adjusted change -7.1 percentage points, p<0.001) and more patients underwent the monofilament test (25.9% vs. 18.7%, adjusted change +12.3 percentage points, p<0.001). Testing for albuminuria remained low (30.3%) in 2014.

Medication (Table 2)

Hyperglycemia was controlled by diet alone in approximately one fourth of the patients in both surveys. There was shift away from insulin in monotherapy towards other therapy schemes between 2005 and 2014 ($p<0.001$), and the overall frequency of the use of insulin also decreased (16.0% vs. 22.2%, adjusted change -4.5 percentage points, $p=0.001$). Significantly more patients were on combination therapy involving more than two agents in 2014 (11.6% vs. 1.9%, adjusted change +8.9 percentage points). Metformin was the most frequently used antihyperglycemic agent in 2014 (63.7%), and the use of metformin had increased substantially since 2005 (46.3%; adjusted change +15.0 percentage points, $p<0.001$). Use of sulfonylureas, on the other hand, was reduced (19.2% vs. 30.6% , adjusted change -11.9 percentage points, $p<0.001$). New glucose-lowering agents were used by more than one-fifth of the patients in 2014.

Sixtysix percent of patients received antihypertensive medication in both study years, however the use of ACE/AII inhibitors, calcium blockers and thiazides all increased (all $p<0.001$) and there was a shift towards increased use of combination therapy . The proportion of patients on lipid lowering medication increased among patients with coronary heart disease (77.9% vs. 67.5%, adjusted change +8.8 percentage points, $p<0.001$) as well as in general (54.5% vs. 43.7%, adjusted change +11.3 percentage points, $p<0.001$).

Measurements and attained treatment targets (Table 3)

The patients achieved significantly more of the 2009 national treatment targets in 2014 than in 2005 ($p<0.001$), even though only 16.1% of patients reached all three targets in 2014. HbA_{1c} ≤7.0% (≤53 mmol/mol) was achieved by 62.8% in 2014 vs. 54.3% of the patients in 2005 (adjusted change +8.0 percentage points, $p<0.001$), although the mean

HbA_{1c} levels declined by only 0.2 percentage points (1.6 mmol/mol) (adjusted; p=0.005). Among patients on diet only, a high proportion of patients attained the HbA_{1c}-target in both study years (87.3% in 2014), and in 2014 an improvement was seen among patients on medication (54.2% vs. 43.9%, adjusted change +8.5 percentage points, p<0.001). The proportion with HbA1c >9.0% (>75 mmol/mol) was fairly stable (5.6% in 2014).

More patients met blood pressure targets (≤135/80 mmHg on antihypertensive medication and ≤140/85 mmHg without medication) in 2014 (50.2% vs. 42.3%, adjusted change +7.2 percentage points, p<0.001), and the mean adjusted systolic blood pressure decreased by 3.3 mmHg (p<0.001).

Substantially more patients also achieved the total cholesterol target (≤4.5 mmol/L) in 2014 (49.9% vs. 33.5%, adjusted change +15.4 percentage points, p<0.001). Among patients on lipid lowering medication, the proportions reaching target total cholesterol were in general higher, and also increasing (65.3% vs. 49.9%, adjusted change +13.7 percentage points, p<0.001). The 2009-treatment target for LDL was met by 51.9% of all patients in 2014, however, among patients with coronary heart disease the proportion with LDL ≤1.8 mmol/L was substantially lower: 29.7%.

Vascular complications (Table 4)

The proportion of patients with coronary heart disease was relatively stable (22.0% in 2014). There was a marked decrease in the proportion with neuropathy and with pathological monofilament test results among the relatively few patients registered with these variables. Chronic kidney disease as evaluated by eGFR<60 ml/min was present in 17.3% of the patients in 2014, whereas 1.7% had eGFR of less than 30 ml/min.

Conclusions

We found clinically important improvements in the percentages attaining recommended targets for HbA_{1c}, blood pressure and lipids in 2014 vs. 2005. However, the recording of screening procedures for microvascular complications remained alarmingly poor. Furthermore, the proportion of current smokers was disturbingly high.

Study samples

We consider our findings to be representative for type 2 diabetes patients treated by GPs in Norway. In both the ROSA 4 and ROSA 3 surveys, data were collected from routine clinical practice with all GPs in a practice participating. Furthermore, patients in the 2014 survey were similar to the type 2 diabetes population in the comprehensive Swedish and Scottish Diabetes Registries in 2014 and with other recently published surveys from Europe and the United States with respect to age, gender, diabetes duration and BMI (9; 14; 15; 18; 32-35).

Processes of care

Recordings of HbA_{1c}, blood pressure, lipids and smoking status in 2014 were acceptable and comparable to other surveys, while recording of weight/BMI was low (14; 15; 36). Screening for microvascular complications was poor and inferior to that found in the diabetes registres from Sweden and Scotland, in the UK National Diabetes Audit, and in cross-sectional studies in the United States (14-16; 36). When comparing the results from ROSA 4 with Sweden, Scotland, United Kingdom (UK) and the United States, the proportions with annual checks for albuminuria were 30% vs. 71-75%, neuropathy 26% vs. 71-94% and eye examination 61% vs. 70-90%. Surprisingly, the percentage of patients with a recorded opthalmological examination was lower in 2014 than in 2005. The differences between Norway and Sweden may be due to

the use of reminders on the fill-in forms used by practices to report to the registry and the availability of diabetes specialist nurses in GP practices in Sweden. In addition, national initiatives in the UK to improve care for people with diabetes may have lead to increasing sceening rates, i.e. the National Service Framework for Diabetes (37). In pediatric diabetes care in Norway, it has been shown that establishement of a nationwide system for benchmarking of quality indicators resulted in significant improvements in risk factor control and screening assessments (38).

In the general population in Norway the percentage of current smokers decreased from 24% in 2004 to 13% in 2014 (39). In contrast the prevalence of current smokers in ROSA 4 remained high, 22.7%, and similar to reports from the American National Health and Nutrition Examination Survey (NHANES) where the prevalence remained unchanged at 22% between 1999-2002 and 2007-2010 (16). Corresponding percentages in Sweden and Scotland in 2014 were 17% and 18% (15; 40). A Swedish study found an excess mortality in type 2 diabetes patients younger than 55 years, and 38% of these were current smokers (9). Motivating diabetes patients to stop smoking should be an important priority for GPs.

Medication, measurements and attained treatment targets

In accordance with national guidelines, the percentage of patients using metformin increased. The use of sulfonylureas decreased substantially (-12 percentage points). The same trends were seen in a recent publication from the United States (35).

Risk factor control has improved during the last decade. The increase in achievement of HbA_{1c} targets were similar to the observations between the periods 1999-2002 and 2007-2010 in NHANES (+8 percentage points) (16). Compared with recent cross-sectional studies or

annual reports from diabetes registries of type 2 diabetes in general practice worldwide, the proportion of patients achieving HbA_{1c} <7.0% (<53 mmol/mol) in ROSA 4 was 57% vs 47-52% (15; 16; 18; 19). This confirmes that glycaemic control in Norwegian general practice is similar to other countries.We only found a slight improvement in mean HbA1c that was similar to findings in reports from the Swedish Diabetes Registry and NHANES (14; 16). The relatively small decline in mean HbA1c seen during the last decade may be due to the reduction of the use of insulin. It is possible that the GPs postpone insulin-treatment, and start with the new expensive antihyperglycemic agents which have less glucose lowering effect than insulin. During recent years guidelines have emphasized the need for individual glycaemic treatment targets for patients with long diabetes duration and comorbidities (27-29). These targets are often less intensive than previously strict recommendations and may also explain the clinically insignificant change in mean HbA_{1c}. Finally, mean HbA1c is now at such a low level that lower mean values are difficult to achieve in large study populations.

The increased use of antihypertensive agents probably explains the improved blood pressure control. However, there is still a high proportion of untreated patients above intervention threshold and treated patients above blood pressure targets. In our present study 38.5% achieved a blood pressure ≤130/80 mmHg (regardless of medication) in 2014. Findings from other countries span from 33.8% (Scotland), 41.6% (Swedish Diabetes Registry), to 51.3% (NHANES) (15; 16; 19).

The improved control of dyslipidemia might be influenced by the introduction of LDL-targets in national guidelines in 2009 (31). The proportion of patients on lipid lowering therapy with cholesterol <4.5 mmol/L were similar in ROSA 4 and the Swedish Diabetes Registry (62.0% vs. 59.0%), while the Swedish had a higher proportion with LDL <2.5 mmol/L (42.3% vs.

52.6%). The use of statins in ROSA 4 was inferior to Sweden (54.5% vs. 63.7%). Only 28.5% of patients with a history of CVD attained LDL target ≤1.8 mmol/L, similar to results from NHANES (27.5%) (16). This indicates that more diabetes patients should start lipid-lowering therapy in Norway and that GPs should maintain efforts to achieve the strict LDL-target in high-risk persons with CVD.

Vascular complications

There was no significant change in the prevalence of coronary heart disease during the last decade in our study populations. This is similar to the findings in two recent cross-sectional surveys from the United States (33; 35). The prevalence of microvascular complications in our study is subject to uncertainty due to poor recording of screening among GPs in both surveys (~ 60% eye examination, ~30% albuminuria test and ~ 25% monofilament test in 2014). We found no significant change in retinopathy between ROSA 4 and ROSA 3, but the 12.3% prevalence of patients with retinopathy in 2014 is probably underestimated due to inconsistent reporting. The Swedish Adult Diabetes Register reports a prevalences of retinopathy of 29.6% in their annual 2014 report. Their findings are probably more representative of retinopathy among type 2 diabetes patients in general practice in Scandinavia (14). Fewer persons had neuropathy in ROSA 4 compared with ROSA 3 while more patients had a recorded monofilament test. This may indicate a selection bias of patients tested with monofilament in 2005. However, the prevalence of neuropathy in 2014 (18.8%) is in agreement with reports from the Swedish National Diabetes Register 2014 (21%), and both countries have ~2.7% with a history of foot ulcer. ROSA 4 and Scotland report similar percentages of lower limb amputation, 0.6% and 0.7%, respectively. ROSA 4 and Scotland have the same proportion of patients with end-stage renal failure, 0.6%.

This study is one of the largest representative cross-sectional studies of type 2 diabetes in general practice performed in recent years, originating from a high-income country with an apparently well-organized healthcare system. Our study has some limitations. Screening procedures for microvascular complications are based on recorded data in the case notes. If GPs fail to record performed procedures our results will overestimate the quality gaps. The level of albuminuria is not reported due to different measurement methods/units between GP practices, and frequent missing data. Finally, we excluded patients with main-follow up in specialist health care who probably had worse glycemic control, however, the absolute numbers were small and unlikely to influence the results (4.4% in 2014 vs. 5.0% in 2005).

In summary, we found moderate improvements in blood pressure- and lipid control during the last decade that are similar to improvements reported from other countries. Improvements during the last decade are less striking than improvements reported in the previous decade. We demonstrated that there are still major gaps in the performance of recommended screening procedures to detect microvascular complications. Clinical performance in this area was considerably worse than other comparable countries. We also found a disturbingly high proportion of current smokers diverging from trends seen in the general Norwegian population. There is still considerable room for improvements of many aspects of diabetes care in general practice. Screening for microvascular complications must be improved. Risk factor control, especially the treatment of dyslipidemia, and the promotion of smoking cessation require attention. We suggest compulsory

reporting to a national diabetes register and feedback to GPs as a means of continually evaluating diabetes control and promoting further improvements in diabetes care in Norway. A national screening program for diabetes retinopathy should also be considered.

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Author Contributions. Å.B. quality checked, analysed the data and performed the statistical analyses, drafted, reviewed and edited the manuscript. J.G.C., A.K.J. conceived the study protocol and analysis plan, applied to the Regional Ethic Comitee, invited GPs and GP practices, contributed to the discussion, reviewed and edited the manuscript. S.Sa., G.T., T.C., A.T.T, B.G., T.J.B., K.F.L., T.V.M. conceived the study protocol and

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Å.B. are the guarantor of this work and as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analyses.

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Processes of care	2014 (n=9464) Percentages		2005 (n=5463) Percentages		Change from 2005 to 2014 with 95% CI ‡ Percentage points
	Observed, with 95% CI †	Adj. ‡	Obs.	Adj. ‡	
HbA_{1c}	86.4 (84.9 to 87.9)	86.8	91.8	91.3	-4.4 (-6.7 to -2.1)**
Blood pressure	87.4 (85.8 to 89.0)	88.1	89.7	88.7	-0.5 (-3.2 to 2.2)
Cholesterol	89.0 (86.8 to 91.2)	89.0	89.5	89.6	-0.6 (-3.7 to 2.4)
LDL	84.4 (81.1 to 87.7)	83.8	40.8	41.7	+42.1 (32.9 to 51.2)**
Creatinine/eGFR	93.2 (91.5 to 95.0)		NA		
Weight	51.4 (46.7 to 56.1)	51.8	54.2	53.6	-1.8 (-12.7 to 9.1)
BMI	44.6 (40.0 to 49.3)	45.1	36.9	36.3	+8.8 (-1.9 to 19.5)
Smoking habits	79.0 (76.2 to 81.9)	79.6	56.0	54.6	+24.9 (18.3 to 31.5)**
Eye examination	61.0 (57.4 to 64.6)	62.3	71.5	69.4	-7.1 (-11.1 to -3.2)**
Albuminuria	30.3 (25.6 to 34.9)	31.3	37.9	36.1	-4.8 (-13.8 to 4.1)
Monofilament 10g	25.9 (21.5 to 30.3)	28.1	18.7	15.8	+12.3 (6.6 to 17.9)**
Number of screening procedures for micro-vascular complications §					**
0	29.2 (25.7 to 32.8)	28.0	21.2	22.8	+5.2 (0.5 to 10.0)
1	36.3 (34.2 to 41.6)	35.5	41.6	43.0	-7.5 (-11.7 to -3.4)
2	22.5 (20.0 to 25.0)	23.0	25.7	24.6	-1.6 (-6.5 to 3.2)
3	12.0 (9.1 to 14.8)	13.4	11.6	9.6	+3.9 (-0.8 to 8.6)

Table 1
Processes of care documented in type 2 diabetes patients in general practice in Norway in 2014 (ROSA 4) and 2005 (ROSA 3).

*p≤0.01, **p≤0.001. NA = not available. Obs.=observed. Adj.=adjusted
† Based on data as registered, 95% CIs adjusted for clustering within GP practices.
‡ Adjusted for sex, age, counties and clustering within GP practices.
§ Screening procedures: Eye examination, albuminuria, 10 gram monofilament test.

Medication	2014 (n=9464) Percentages		2005 (n=5463) Percentages		Change from 2005 to 2014 with 95% CI ‡ Percentage points
	Observed, with 95% CI †	Adj. ‡	Obs.	Adj. ‡	
Antihyperglycemic therapy					**
Diet only	27.4 (24.4 to 30.4)	28.3	28.2	26.8	+1.5 (-2.8 to 5.9)
Antihyperglycemic agents except for insulin	56.6 (53.9 to 59.2)	55.1	49.6	52.3	+2.7 (-1.2 to 6.7)
Insulin only	4.9 (4.3 to 5.5)	5.0	12.4	11.7	-6.7 (-8.6 to -4.8)
Insulin combined with other antihyperglycemic agents	11.2 (10.2 to 12.2)	11.6	9.7	9.2	+2.4 (1.1 to 3.8)
Groups of antihyperglycemic agents					
Metformin	63.7 (60.6 to 66.8)	62.9	46.3	47.8	+15.0 (10.7 to 19.4)**
Sulfonylurea	19.2 (17.5 to 20.9)	19.1	30.6	31.0	-11.9 (-15.2 to -8.5)**
Insulin	16.0 (14.8 to 17.3)	16.6	22.2	21.1	-4.5 (-7.0 to -2.0)**
DPP-4-inhibitors	15.9 (13.8 to 18.0)		NA		
GLP1-analogs	3.1 (2.6 to 3.7)		NA		
SGLT2-inhibitors	3.5 (2.5 to 4.4)		NA		
Numbers of antihyperglycemic agents, insulin included					**
1	37.2 (35.3 to 39.2)	37.1	43.8	44.5	-7.4 (-10.7 to -4.1)
2	23.8 (22.4 to 25.1)	23.6	26.2	26.8	-3.2 (-5.7 to -0.7)
≥ 3	11.6 (10.5 to 12.7)	11.0	1.9	2.1	+8.9 (7.9 to 10.0)
Antihypertensive agents					
Antihypertensives	66.0 (63.3 to 68.7)	66.0	66.4	66.4	-0.4 (-3.8 to 3.0)
ACE/AII inhibitors	52.6 (50.3 to 54.9)	52.9	47.4	46.8	+6.2 (2.5 to 9.8)**
Beta blockers	30.5 (28.7 to 32.4)	30.7	31.2	30.9	-0.3 (-3.0 to 2.5)
Calsium blockers	25.9 (24.1 to 27.7)	26.6	22.2	21.2	+5.4 (2.9 to 8.9)**
Thiazides	27.2 (25.4 to 28.9)	27.8	22.0	21.1	+6.7 (3.9 to 9.4)**
Numbers of antihypertensives					**
1	19.2 (18.2 to 20.2)	19.1	21.7	21.8	-2.7 (-4.6 to -0.9)
2	20.4 (19.3 to 21.4)	20.2	21.2	21.4	-1.2 (-3.2 to 0.8)
3	16.2 (15.2 to 17.3)	16.4	15.0	14.7	+1.7 (0.1 to 3.4)
≥4	10.2 (9.1 to 11.4)	10.7	8.5	7.9	+2.9 (1.2 to 4.5)
Lipid lowering medication	54.5 (51.9 to 57.2)	54.7	43.7	43.4	+11.3 (7.1 to 15.5)**
with CHD	77.9 (74.3 to 81.5)	77.3	67.5	68.5	+8.8 (3.4 to 14.2)**
Antithrombotic therapy	36.9 (34.7 to 39.2)	37.3	40.0	39.4	-2.2 (-5.7 to 1.3)

Table 2
Overview of antihyperglycemic-, antihypertensive-, lipid lowering- and antiplatelet therapy in type 2 diabetes patients in general practice in Norway in 2014 (ROSA 4) and 2005 (ROSA 3).

* p≤0.01, **p≤0.001, NA = not available. Obs.=observed. Adj.=adjusted.
CHD=coronary heart disease.
† Based on data as registered, 95% CIs adjusted for clustering within GP practices.
‡ Adjusted for sex, age, counties and clustering within GP practices.
Medication was extracted from the GP's electronical prescriptions. For antithrombotic therapy 0.6% (n=33) were missing in 2005, for all other medication groups data was available in 100% of the cases.

Measurements and attained targets		2014 (n=9464) Means or percentages		2005 (n=5463) Means or percentages		Change from 2005 to 2014 with 95% CI ‡ Means or percentage points
Measurements	Valid cases 2014/2005 (%)	Observed, with 95% CI †	Adj. ‡	Obs.	Adj. ‡	
HbA_{1c}						
%	86/92	7.0 (6.9 to 7.1)	7.0	7.1	7.1	-0.2 (-0.3 to -0.0)*
mmol/mol	86/92	52.9 (52.2 to 53.5)	52.9	54.6	54.5	-1.6 (-2.9 to -0.4)*
SBP (mmHg)	87/90	135.1 (134.2 to 136.0)	138.9	135.3	138.6	-3.3 (-4.8 to -1.8)**
DBP (mmHg)	86/90	78.0 (77.5 to 78.4)	78.9	77.9	79.0	-1.1 (-1.9 to -0.2)*
Chol (mmol/L)	89/89	4.7 (4.6 to 4.7)	4.7	5.1	5.1	-0.4 (-0.5 to -0.3)**
LDL (mmol/L)	84/41	2.8 (2.7 to 2.8)	2.8	3.1	3.1	-0.3 (-0.4 to -0.3)**
Targets						
HbA_{1c} (%)(mmol/mol)						
≤ 7.0 (≤53)	86/92	62.8 (60.6 to 65.0)	62.6	54.3	54.6	+8.0 (3.8 to 12.1)**
Diet only	82/86	87.3 (84.8 to 89.8)	87.5	83.5	83.2	+4.3 (0.5 to 8.1)
Medicated	88/94	54.2 (51.8 to 56.7)	53.5	43.9	45.1	+8.5 (3.8 to 13.1)**
> 9.0 (>75)	86/92	5.6 (4.7 to 6.4)	5.6	6.9	6.9	-1.3 (-2.6 to – 0.0)
Blood pressure						
≤ 135/80 mmHg	87/90	44.9 (41.9 to 47.9)	44.7	36.6	37.0	+7.7 (3.2 to 12.2)**
Medicated	92/94	41.3 (38.5 to 44.2)	41.1	31.2	31.5	+9.5 (5.1 to 14.0)**
>140/85 mmHg, Unmedicated	79/82	29.6 (26.0 to 33.1)	29.5	32.3	32.4	-2.8 (-8.2 to 2.6)
Comb.target §	87/90	50.2 (47.5 to 53.0)	50.0	42.3	42.8	+7.2 (2.8 to 11.5)**
Lipids (mmol/L)						
Chol ≤ 4.5	89/89	49.9(48.2 to 51.6)	49.5	33.5	34.1	+15.4(12.2 to 18.6)**
Medicated	94/96	65.3 (63.6 to 67.0)	64.8	49.9	51.0	+13.7(10.0 to 17.4)**
LDL≤2.5	84/41	46.3 (44.5 to 48.1)	46.1	29.3	29.8	+16.3(12.4 to 20.2)**
Medicated	90/44	62.3 (60.7 to 64.0)	62.1	44.8	46.1	+16.0(10.8 to 21.1)**
LDL ≤1.8 With CHD	85/36	29.7 (27.3 to 32.0)	29.2	13.0	13.9	+15.3(11.8 to 18.7)**
LDL target 2009‖	82/21	51.9 (50.3 to 53.5)	51.8	6.4	6.6	+45.2(43.2 to 47.2)**
Attained targets¶	75/79					**
0		10.5 (9.5 to 11.6)	10.6	19.7	19.5	-8.9 (-11.2 to -6.5)
1		35.0 (33.3 to 36.7)	35.3	42.7	42.3	-7.0 (-9.6 to -4.4)
2		38.4 (37.1 to 39.7)	38.1	30.2	30.8	+7.3 (4.9 to 9.7)
3		16.1 (14.6 to 17.5)	16.1	7.4	7.5	+8.6 (6.5 to 10.7)

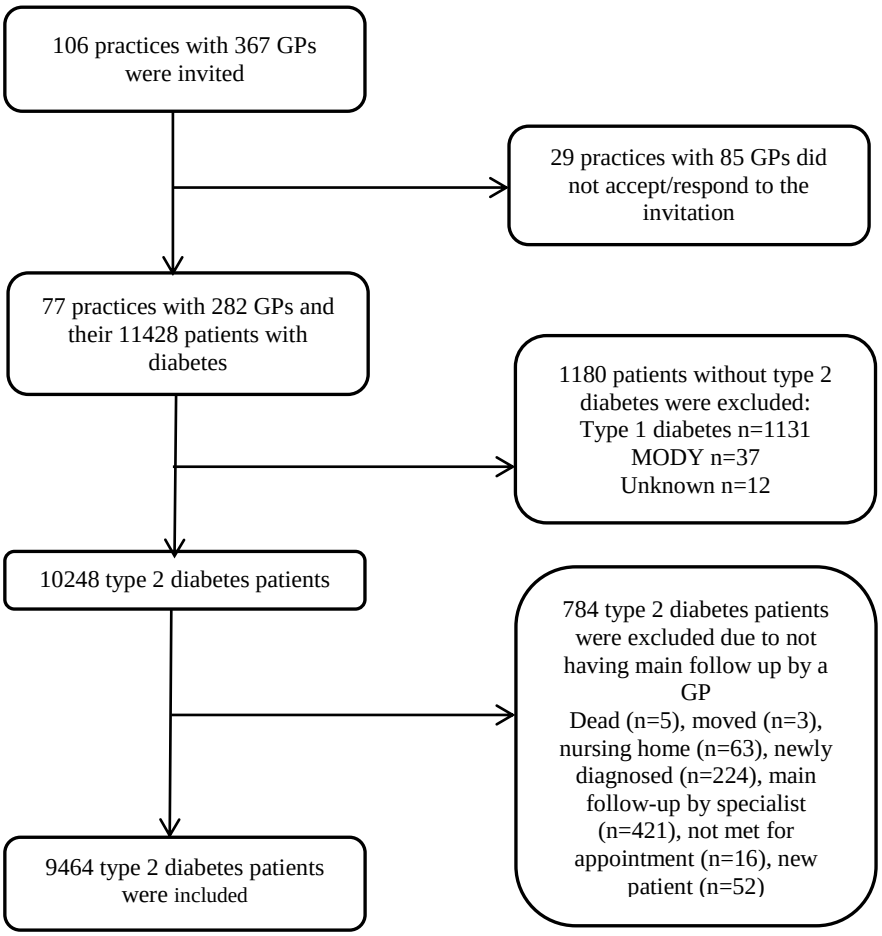
Table 3
Measurements and attained treatment targets in type 2 diabetes in general practice in Norway in 2014 (ROSA 4) and 2005 (ROSA 3).

*p≤0.01**, p≤0.001. Obs.=observed. Adj.=adjusted.
SBP=systolic blood pressure. DBP=diastolic blood pressure. CHD=coronary heart disease.
† Based on data as registered, 95% CIs were adjusted for clustering within GP practices.
‡ Adjusted for sex, age, county and clustering within GP practices.
§ Combined target: ≤ 135/80 mmHg with antihypertensives or ≤140/85 mmHg without antihypertensives
‖ For patients with cardiovascular disease: LDL≤ 1.8 mmol/L, without cardiovascular disease; ≤ 2.5 mmol/L on lipid lowering therapy, ≤3.5 mmol/L without lipid lowering therapy
¶ For patients that have measured all of HbA1c, blood pressure and lipids: HbA1c ≤7.0% (53 mmol/mol), blood pressure ≤135/80 mmHg, cholesterol ≤4.5 mmol/L

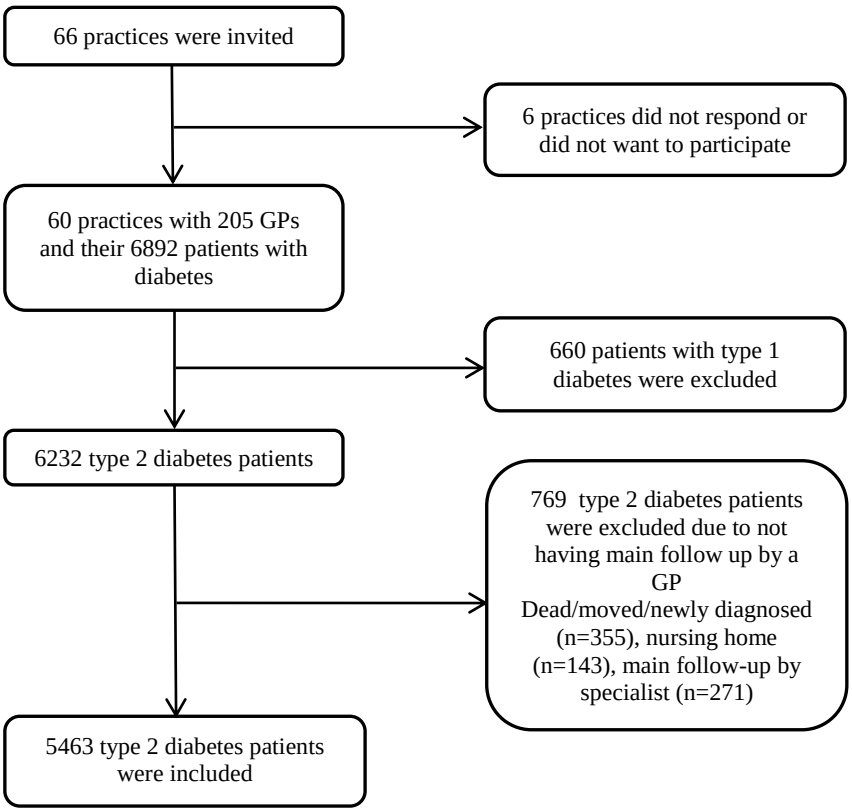
Complications		2014 (n=9464) Percentages		2005 (n=5463) Percentages		Change from 2005 to 2014 with 95% CI ‡
Microvascular complications	Valid cases 2014/2005 (%)	Observed, with 95% CI †	Adj. ‡	Obs.	Adj. ‡	
Retinopathy §	60/60	12.3 (11.1 to 13.4)	12.2	14.6	14.8	-2.6 (-5.1 to -0.1)
Neuropathy ‖	28/21	18.8 (15.8 to 21.8)	17.8	33.2	37.4	-19.6 (-25.5 to -13.7)**
Pathological monofilament ¶	26/19	10.6 (8.2 to 13.1)	10.0	21.4	25.0	-15.0 (-21.5 to -8.6)**
Foot ulcer	100/100	2.7 (2.1 to 3.2)	2.6	3.3	3.4	-0.8 (-1.7 to 0.2)
Lower limb amputation	100/100	0.6 (0.5 to 0.8)	0.6	0.4	0.5	+0.1 (-0.1 to 0.4)
Nephropathy						
Dialysis	100/100	0.2 (0.1 to 0.3)		NA		
Kidney tx	100/100	0.2 (0.1 to 0.3)		NA		
CKD-stage (eGFR, ml/min)	93/NA					
45-59		11.2 (10.2 to 12.1)		NA		
30-44		4.4 (3.8 to 5.0)		NA		
15-29		1.5 (1.2 to 1.8)		NA		
< 15		0.2 (0.1 to 0.3)		NA		
Macrovascular complications						
Coronary heart disease#	100/100	22.0 (21.0 to 22.9)	22.7	25.7	24.3	-1.6 (-3.2 to 0.0)
Stroke ‡‡	100/100	7.3 (6.6 to 7.9)	7.4	10.2	10.0	-2.6 (-3.8 to -1.3)**
PTA/art. surgery	100/100	2.0 (1.6 to 2.3)		NA		

Table 4
Vascular complications of type 2 diabetes patients in general practice in Norway in 2014 (ROSA 4) compared with 2005 (ROSA 3).

*≤0.01, **p≤0.001. NA= not available. Obs.=observed. Adj.=adjusted. Kidney tx= kidney transplantation. CKD=chronic kidney disease, eGFR=estimated glomerulofiltrationrate, PTA/art.surgery: Percutaneous transluminal angioplasty or arterial surgery
† Based on data as registered, 95% CIs adjusted for clustering within GP practices.
‡ Adjusted for sex, age, county and clustering within GP practices.
§ Non-proliferative/proliferative retinopathy stated in case notes regardless of time. Macular edema excluded.
‖ Pathological monofilament test or foot ulcer or lower limb amputation
¶ Pathological monofilament test ≥1/8.
# Coronary heart disease: Myocardial infarction, angina, revascularization.
‡‡ Stroke: Ischemic attack, transient ischemic attacks excluded in 2014, included in 2005.



Supplemental Figure S1
Flowchart of general practices and patients with type 2 diabetes included in ROSA 4 (2014).
GPs= General practitioners. MODY=maturity onset diabetes of the young.



Supplemental Figure S2
Flowchart of general practices and patients included in ROSA 3 (2005).
GPs= General practitioners.

Variables	ROSA 4 (2014)	ROSA 3 (2005)
Characteristics		
Diabetes duration	2014 minus year of diagnosis	2005 minus year of diagnosis
Ethnicity	Caucasians or others	Caucasians or others
Height	If ever registered	If ever registered
Weight	15 months	12 months
BMI	15 months	12 months
Current smokers	*No;* if ever registered as non-smoker. *Yes*; if registered as current smoker the last 5 years and not changed smoking status	*No;* if ever registered as non-smoker. *Yes*; if registered as current smoker the last 3 years
Complications		
Microvascular complications		
Retinopathy	If ever registered	If ever registered
Reduced foot sensibility	If ever registered	If ever registered
Macrovascular complications		
Coronary heart disease	If ever registered	If ever registered
Stroke	If ever registered apoplexia cerebri	If ever registered apoplexia cerebri or TIA
Diabetic foot ulcer	If ever registered	If ever registered
Processes of care		
HbA1c	12 months	12 months
Blood pressure	15 months	12 months
Lipids	36 months	36 months
Creatinine/eGFR	36 months	
Documentation of smoking status	Non-smokers if ever registered. Smokers 5 years	Non-smokers if ever registered. Smokers 36 months.
Microvascular screening		
Reduced foot sensibility	15 months	12 months
Urin albumin	12 months	12 months
Eye examination	Eye examination 24 months, referral eye specialist 30 months	Eye examination or referral to eye specialist 24 months
Medication		
	Digitally extracted prescriptions 15 months	Digitally extracted prescriptions

Supplemental Table S1
Variables extraction in the ROSA 4 survey (2014) and ROSA 3 survey (2005).
Retinopathy: Non-proliferative and proliferative retinopathy regardless of treatment, macula oedema excluded.
Reduced foot sensibility: Pathological monofilament test and/or any form of vibration test
Monofilament test: 10-g monofilament, pathological if abscense of sensation of $\geq$1 of 8 touches
Coronary heart disease: Acute myocardial infarction, angina, percutaneous coronary intervention/coronary artery bypass surgery. TIA: Transient ishemic attacks
2014: 12 months (Jan. 1st to Dec. 31st 2014), 15 months (Oct. 1st 2013 to Dec. 31st 2014), 24 months (Jan. 1st 2004 to Dec. 31st 2005), 30 months (July 1st 2012 to Dec. 31st 2014).
2005: 12 months (Jan. 1st to Dec. 31st 2005), 24 months (Jan 1st 2004 to Dec. 31st 2005), 36 months (Jan. 1st 2003 to Dec.31st 2005)

Characteristics	Valid cases 2014/2005 n (%)	2014 (n=9464)	2005 (n=5463)
Male (%)	100/100	54.6	50.4
Age (years)	100/100	66.0 (48.0 to 82.0)	65.9 (48.0 to 83.0)
Caucasian (%)	99/100	86.3	89.7
Current smokers (%)	79/57	22.7	25.2
Urban (%)	100/100	85.2	80.4
Diabetes duration (years)	94/94	7.0 (1.0 to 18.0)	5.0 (1.0 to 14.0)
BMI (kg/m^2)	45/37	29.2 (23.6 to 37.7)	29.0 (23.2 to 37.2)
Bariatric surgery (%)	100/ NA	1.5	NA

Supplemental Table S2
Characteristics of type 2 diabetes patients in general practice in Norway in 2014 (ROSA 4) compared with 2005 (ROSA 3).

Values given as median (10-90 percentiles) unless otherwise noted. NA=not available.