Research: Care Delivery

Variation in the achievement of HbA1c, blood pressure and LDL cholesterol targets in type 2 diabetes in general practice and characteristics associated with risk factor control

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Aims To identify population, general practitioner, and practice characteristics associated with the achievement of HbA1c, blood pressure and LDL cholesterol targets, and to describe variation in the achievement of risk factor control.

Methods We conducted a cross-sectional survey of 9342 people with type 2 diabetes, 281 general practitioners and 77 general practices in Norway. Missing values (7.4%) were imputed using multiple imputation by chained equations. We used three-level logistic regression with the achievement of HbA1c, blood pressure and LDL cholesterol targets as dependent variables, and factors related to population, general practitioners, and practices as independent variables.

Results Treatment targets were achieved for HbA1c in 64%, blood pressure in 50%, and LDL cholesterol in 52% of people with type 2 diabetes, and 17% met all three targets. There was substantial heterogeneity in target achievement among general practitioners and among practices; the estimated proportion of a GPs diabetes population at target was 55–73% (10–90 percentiles) for HbA1c, 36–63% for blood pressure, and 47–57% for LDL cholesterol targets. The models explained 11%, 5% and 14%, respectively, of the total variation in the achievement of HbA1c, blood pressure and LDL cholesterol targets. Use among general practitioners of a structured diabetes form was associated with 23% higher odds of achieving the HbA1c target (odds ratio 1.23, 95% confidence interval (CI) 1.02–1.47) and 17% higher odds of achieving the LDL cholesterol target (odds ratio 1.17, 95% CI 1.01–1.35).

Conclusions Clinical diabetes management is difficult, and few people meet all three risk factor control targets. The proportion of people reaching target varied among general practitioners and practices. Several population, general practitioner and practice characteristics only explained a small part of the total variation. The use of a structured diabetes form is recommended.

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Introduction

People with type 2 diabetes have a doubled risk of death and cardiovascular disease compared with the general population [1]. The risk increases with each risk factor above target [2]. A meta-analysis of randomized controlled trials (RCTs) has shown a linear relationship between the reduction in HbA1c and major cardiovascular events [3]. Another meta-analysis of RCTs, showed that reaching blood pressure targets was associated with decreased risk of diabetes-related mortality [4]. Additionally, very low LDL cholesterol level was associated with reduced cardiovascular risk in people with type 2 diabetes [5]. It is therefore important for people with diabetes to achieve HbA1c, blood pressure and LDL cholesterol targets.

Healthcare services in Norway are state-funded. Each member of the population is listed with one specific general practitioner (GP). GPs provide care for most individuals with type 2 diabetes; however, they do not receive financial incentives for the provision of a high quality of clinical care.
In a recent study, we found major gaps between national diabetes guidelines and the performance of screening to detect microvascular complications, with significant heterogeneity among GPs within general practices [6]. The aim of the present study was to examine how population characteristics and available GP and practice characteristics were associated with the achievement of HbA1c, blood pressure and LDL cholesterol targets. In addition, we describe variation in the achievement of targets.

Participants and methods

We used data from the ROSA 4 study, a cross-sectional survey designed to assess the quality of diabetes care in general practice in Norway in 2014. Veriﬁed and representative data from electronic health records in three of the four health regions in Norway were collected and are described in detail elsewhere [6].

In the present study we included 9342 adults (age ≥18 years) with type 2 diabetes (T90 in the International Classiﬁcation of Primary Care) who had their main follow-up in their general practice, and who had a diabetes duration of ≥6 months (Fig. 1). The included population was treated by 281 GPs at 77 practices (73% and 77%, respectively, of those invited to contribute data). Socio-economic variables were obtained from Statistics Norway. Two questionnaires were used to gather GP and practice characteristics (completed in 99% and 100% of cases).

The outcome variables were deﬁned according to national guidelines from 2009: HbA1c ≤53 mmol/mol (≤7.0%), blood pressure ≤135/80 mmHg/≤140/85 mmHg (with/without anti-hypertensive medication) and LDL cholesterol ≤1.8 mmol/l with cardiovascular disease, or ≤2.5/≤3.5 mmol/l without cardiovascular disease with/without lipid-lowering medication. We used the most recent target value between 1 October 2013 and 31 December 2014, although, if none was available, the search period was extended backwards to 1 January 2012 (7.8% of HbA1c measurements and 19.1% of LDL cholesterol measurements).

As explanatory variables, we included 12 diabetes population characteristics (demographics, socio-economic status, complications), 10 GP characteristics (demographics, speciality status and proxies for workload and routines), and four practice characteristics (location, proxies for practice size and routines); Table 1a,b.

Statistical analyses

Descriptive statistics are presented as medians with 10th and 90th percentiles for continuous variables, and counts and percentages for categorical variables. Missing information regarding individuals with diabetes (7.4%) was imputed using multiple imputation by chained equations with predictive mean matching, allowing for the multilevel structure of the data [7]. In addition to the variables in the main models, the imputations included the following as auxiliary variables: weight; height; HbA1c; systolic blood pressure; diastolic blood pressure; total cholesterol; HDL cholesterol; LDL cholesterol; triglycerides; retinopathy; atrial fibrillation; dialysis; and kidney transplantation. We produced 100 imputed datasets. Furthermore, number of years practising in Norway was unknown for 11 GPs, and was single-imputed based on the year of Norwegian authorization, which was known for all GPs.

The associations between the outcomes and population, GP and practice characteristics were analysed in three-level logistic regression models including random intercepts for GPs (level 2) and practices (level 3). Continuous explanatory variables with severely non-linear effects on the log-odds were analysed on a categorized scale. Variance inﬂation factors were estimated to check for multicollinearity. We report odds ratios (ORs) with 95% CIs for the achievement of targets. Because of the large sample size and multiple testing, corresponding chi-squared P values ≤0.01 for population characteristics and ≤0.05 for GP and practice characteristics were considered statistically signiﬁcant. The models were ﬁtted using adaptive Gaussian quadrature with seven integration points. Results from the imputed datasets were averaged by Rubin’s rules.

The proportion of variance explained by each full model was estimated from the variance of the linear predictor for the ﬁxed portion of the model and from the estimated random intercepts variances [8].

Heterogeneity in the achievement of targets among GPs within practices was illustrated by means of ‘caterpillar’ plots of empirical Bayes estimates of target achievement proportions, obtained from three-level models without ﬁxed effects.
fitted to the original data, and with percentiles from the empirical Bayes distributions. The total variation in the plots reflects the sum of GP and practice random effects. Furthermore, median ORs were calculated from the estimated random intercept variances to quantify the cluster heterogeneity [9], and are presented for GPs, practices, and GPs and practices combined.

Finally, intraclass correlation coefficients were used to estimate the proportion of outcome or residual variation attributed to GPs, practices, and GPs and practices combined. Supplementary analyses included linear regression analysis with continuous outcomes and complete-case analysis. The Venn diagram was made in PYTHON version 3.7 with package matplotlib. Imputation was performed in R version 3.4 with packages mice and miceadds. For the regression modelling, STATA version 15.1 was used with functions mi estimate, melogit, mixed, and mimrgns.

Ethics
The study was approved by the Regional Health Committee in Norway (REK 2014/1374, REK Vest).

Results
The included population (n=9342; Fig. 1) was treated by 281 GPs at 77 practices (Table 1a,b). For the diabetes population in which HbA1c, blood pressure and LDL cholesterol values were available for all (n=7086), 64% achieved the HbA1c target, 50% the blood pressure target and 52% the LDL cholesterol target, and 17% met all three targets (Fig. 2). The median (10th–90th percentile) values were as follows: HbA1c 51 (40–68) mmol/mol [6.8 (5.8–8.4%)]; systolic blood pressure 134 (116–156) mmHg; diastolic blood pressure 80 (66–90) mmHg; and LDL cholesterol 2.6 (1.6–4.0).

HbA1c
Compared with people in the age group 60–69 years, those aged <50 years were less likely to achieve the HbA1c target (OR 0.60, 95% CI 0.51–0.71), while those aged ≥70 years were more likely to achieve the target (Table 2a). Men, people born outside Western Europe, and people with obesity had lower odds of attaining the target. Long diabetes duration was also negatively associated with the achievement of HbA1c target (OR 0.65, 95% CI 0.62–0.67) per 5-year increase. People who had undergone bariatric surgery had almost three times higher odds of attaining the HbA1c target (OR 2.78, 95% CI 1.82–4.25). People attending GPs who were regular users of a structured diabetes form had 23% higher odds of attaining the HbA1c target, (OR 1.23, 95% CI 1.02–1.47; Table 2b).

Blood pressure
People aged < 50 years were more likely to achieve blood pressure targets (OR 1.49, 95% CI 1.26–1.77). Non-Western ethnicity was positively associated with the achievement of the blood pressure target, in particular South Asian ethnicity (OR 1.99, 95% CI 1.61–2.46). Current smokers had higher odds of achieving the blood pressure target (OR 1.20, 95% CI 1.05–1.38). Obese people had reduced odds of achieving the target (OR 0.76, 95% CI 0.66–0.87), while those with BMI < 25 kg/m² had increased odds of attaining blood pressure targets.
pressure target compared with those with BMI 25–29.9 kg/m² (OR 1.40, 95% CI 1.17–1.68). No GP or practice characteristics were associated with the achievement of the blood pressure target in our model.

**LDL cholesterol**

Men had higher odds of achieving the LDL cholesterol target compared with women (OR 1.51, 95% CI 1.36–1.67). A positive association with the achievement of LDL cholesterol target was found in people of other ethnicity compared with those of Western European/North American and South Asian ethnicity (OR 1.39, 95% CI 1.16–1.66) and ex-smokers (OR 1.24, 95% CI 1.09–1.40). For each 5-year increase in diabetes duration, the odds of reaching the LDL cholesterol target increased by 18% (OR 1.18, 95% CI 1.13–1.23). People with macrovascular complications were less likely to achieve the LDL cholesterol target (OR 0.20, 95% CI 0.18–0.22). GP users of a structured diabetes form had 17% higher odds of getting the individuals with diabetes to the LDL cholesterol target (OR 0.20, 95% CI 0.18–0.22).

**Supplementary analyses**

In supplementary analyses, models with continuous outcomes mostly paralleled results from the logistic regression.
analysis (Table S1). Predicted probabilities are presented in Table S2. In the complete-case analyses (n=3530 for HbA1c target, n=3462 for blood pressure target, n=3308 for LDL cholesterol target; data not shown), there were only minor changes in the effect estimates, that is, the effect of using a diabetes form was slightly reduced, in particular for achieving the LDL cholesterol target which was non-significant. In analyses excluding people aged ≥80 years, the results were similar to the full model (data not shown).

Variation

The fixed effects of the full model explained 11% of the variation in achievement of HbA1c target, whereas fixed and random effects together explained 16% of the variation. The corresponding results for the blood pressure target were 5% and 11%, and for LDL cholesterol target 14% and 16%.

We found statistically significant variation among GPs and among practices for all targets. Figures 3a–c show the variation in predicted proportions of target achievement for the individual GPs within practices. For the HbA1c target, 80% of GPs within practices were predicted to lie between 55% and 73% target achievement. For blood pressure target the variation was bigger, with the 10th to 90th percentile predicted target achievement range being 36% to 63%; whereas for LDL cholesterol the corresponding range was 47% to 57%.

Similarly, individuals treated by a well-performing GP within a well-performing practice had a median 50% higher odds of HbA1c target achievement than those treated by a GP with poorer performance at a practice with poorer results (median OR 1.50, 95% CI 1.36–1.73). For blood pressure and LDL cholesterol targets the corresponding median ORs were 1.61 (95% CI 1.45–1.85) and 1.28 (95% CI 1.19–1.53), respectively. Apart from for LDL cholesterol, the heterogeneity was distributed relatively evenly between GPs and practices, and changed only slightly when adjusting for population, GP and practice factors (Table S3).

By contrast, the residual variation in target achievement was mostly between individuals. The unconditional combined intraclass correlation coefficients for GPs within practices were 5.3 (95% CI 3.7–7.5)% for the HbA1c, blood pressure and LDL cholesterol targets, respectively, and the conditional intraclass correlation coefficients from adjusted models were similar.

Discussion

Clinical management of diabetes is difficult, and only one in five achieved all three targets for HbA1c, blood pressure and LDL cholesterol. This is one of few studies with several explanatory variables on three levels that aim to explore variation in, and factors associated with, the achievement of targets [11]. Young people (age <30 years), people with obesity and those with long diabetes duration were less likely to achieve the HbA1c target, while people with macrovascular disease had lower odds of achieving the LDL cholesterol target. We observed that a small positive effect on the achievement of HbA1c and LDL cholesterol targets was related to GP usage of a structured diabetes form. After adjusting for case mix, there was a moderate residual heterogeneity in target achievement among GPs within
practices, which could only partly be explained by the studied GP and practice characteristics.

We observed that younger people had worse glycaemic control than people aged >60 years. This finding has also been reported in other countries [12,13]. A large observational study in Sweden showed that people with type 2 diabetes aged <55 years had the highest increase in risk of cardiovascular disease and death compared with similarly aged controls [2]. HbA1c level outside target range was also a strong predictor for all cardiovascular outcomes [2].

People with macrovascular complications had low odds of attaining the LDL cholesterol target. In the randomized IMPROVE-IT trial, very low LDL cholesterol levels in people with type 2 diabetes and acute coronary syndrome reduced the incidence of cardiovascular outcomes after 7 years follow-up [5]. Thus, intensification of lipid-lowering therapy among individuals with a history of macrovascular disease should be prioritized.

In the present study, obese people were less likely to achieve HbA1c and blood pressure targets. In the ADDITION-Cambridge trial, weight loss in the first year following a diabetes diagnosis was associated with reduced incidence of cardiovascular disease [14]. Initial weight loss in people with newly diagnosed type 2 diabetes should therefore be encouraged.

We did not measure adherence to medical or lifestyle advice, motivation for lifestyle changes, individual preferences or hypoglycaemic episodes. Poor medication adherence has been identified as a major cause for the observed efficacy gap in HbA1c reduction between RCTs and the real world [15]. A Danish study showed that low frequency of self-monitoring of blood glucose, perceived low treatment efficacy, low adherence, and low primary care utilization were associated with high levels of HbA1c and LDL cholesterol [16].

### Table 2a: Characteristics of people with type 2 diabetes with adjusted odds ratios for the achievement of HbA1c, blood pressure or LDL cholesterol target

| Characteristics                          | HbA1c target† | Blood pressure target‡ | LDL cholesterol target§ |
|-----------------------------------------|---------------|------------------------|-------------------------|
|                                         | OR (95% CI)   | P                      | OR (95% CI)              | P                      | OR (95% CI)              | P                      |
| N = 9342                                |               |                        |                         |                        |                         |                        |
| Men                                     | 0.87 (0.79, 0.96) | 0.005                        | 0.96 (0.87, 1.06) | 0.43                        | 1.51 (1.36, 1.67) | <0.001                        |
| Age < 50 years                          | 0.60 (0.51, 0.71) | <0.001                        | 1.49 (1.26, 1.77) | <0.001                        | 1.11 (0.94, 1.31) | 0.23                        |
| 50–59 years                             | 0.72 (0.63, 0.82) | <0.001                        | 1.15 (1.01, 1.32) | 0.038                        | 0.95 (0.83, 1.09) | 0.47                        |
| 60–69 years                             | 1              | 1                        | 1.11 (0.99, 1.24) | 0.075                        | 0.20 (0.18, 0.22) | <0.001                        |
| 70–79 years                             | 1.36 (1.19, 1.56) | <0.001                        | 0.84 (0.74, 0.96) | 0.009                        | 1.18 (1.03, 1.34) | 0.015                        |
| ≥ 80 years                              | 1.26 (1.06, 1.51) | 0.010                        | 0.69 (0.58, 0.82) | <0.001                        | 1.21 (1.01, 1.45) | 0.04                        |
| Ethnicity                               |               |                        |                         |                        |                         |                        |
| Western European/North American*        | 1              | 1                        | 1.48 (1.24, 1.78) | <0.001                        | 1.39 (1.16, 1.66) | <0.001                        |
| South Asian†                            | 0.66 (0.54, 0.80) | <0.001                        | 1.99 (1.61, 2.46) | <0.001                        | 1.28 (1.04, 1.56) | 0.019                        |
| Other                                   | 0.67 (0.56, 0.79) | <0.001                        | 1.48 (1.24, 1.78) | <0.001                        | 1.18 (1.03, 1.34) | <0.001                        |
| Smoking status                          |               |                        |                         |                        |                         |                        |
| Never smoked                            | 1              | 1                        | 1.10 (0.98, 1.24) | 0.12                         | 1.24 (1.09, 1.40) | 0.001                        |
| Ex-smoker                               | 1.07 (0.95, 1.21) | 0.29                        | 1.20 (1.05, 1.38) | 0.009                        | 1.00 (0.86, 1.15) | 0.96                        |
| Current smoker                          | 0.90 (0.79, 1.04) | 0.15                        |                      |                         |                      |                        |
| BMI < 25 kg/m²                           | 1.20 (1.00, 1.45) | 0.056                        | 1.40 (1.17, 1.68) | <0.001                        | 1.08 (0.82, 1.34) | 0.58                        |
| 25–29.9 kg/m²                           | 0.78 (0.67, 0.91) | 0.002                        | 0.76 (0.66, 0.87) | <0.001                        | 0.94 (0.76, 1.17) | 0.57                        |
| ≥ 30 kg/m²                              | 1              | 1                        | 1.36 (0.92, 2.00) | 0.13                         | 1.61 (1.08, 2.38) | 0.018                        |
| Bariatric surgery                       | 2.78 (1.82, 4.25) | <0.001                        | 1.11 (0.99, 1.24) | 0.075                         | 0.20 (0.18, 0.22) | <0.001                        |
| Macrovascular complications†            | 0.92 (0.82, 1.03) | 0.15                        | 0.74 (0.54, 1.03) | 0.071                         | 1.07 (0.76, 1.50) | 0.71                        |
| Foot ulcer                              | 0.80 (0.59, 1.09) | 0.16                        | 1.34 (0.67, 2.70) | 0.41                          | 0.96 (0.47, 1.95) | 0.90                        |
| Lower limb amputation                   | 0.58 (0.30, 0.15) | 0.12                        | 1.11 (0.99, 1.24) | 0.075                         | 0.20 (0.18, 0.22) | <0.001                        |
| Estimated GFR                           |               |                        |                         |                        |                         |                        |
| > 60 ml/min/1.73 m²                     | 1              | 1                        | 1.05 (0.83, 1.33) | 0.66                          | 0.87 (0.68, 1.22) | 0.12                        |
| 45–59 ml/min/1.73 m²                    | 0.95 (0.80, 1.14) | 0.59                        | 0.92 (0.78, 1.09) | 0.35                          | 1.08 (0.90, 1.28) | 0.40                        |
| 30–44 ml/min/1.73 m²                    | 0.78 (0.61, 0.98) | 0.04                        | 1.05 (0.83, 1.33) | 0.66                          | 0.87 (0.68, 1.22) | 0.12                        |
| <30 ml/min/1.73 m²                      | 0.86 (0.60, 1.24) | 0.43                        | 0.99 (0.69, 1.41) | 0.94                          | 1.13 (0.76, 1.67) | 0.55                        |

GP: general practitioner.
*Adjusted for all population, GP and practice characteristics included in Tables 2a and 2b. †HbA1c ≤ 53 mmol/mol (≤7.0%). ‡Blood pressure ≤135/80 mmHg/≤140/85 mmHg (with/without antihypertensive medication). §LDL cholesterol ≤1.8 mmol/l with cardiovascular disease, or without cardiovascular disease; ≤2.5/≤3.5 mmol/l with/without lipid-lowering medication. ¶Born in Western Europe or North America. **Born in Bangladesh, India, Pakistan or Sri-Lanka. ††Composite variable of either coronary heart disease, stroke and/or peripheral arterial surgery.

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monotherapy, two-thirds successfully [17]. A justifiable source of variation is individualized targets due to multi-morbidity and short life expectancy, individual preferences and resources. Personalized treatment leads to a higher morbidity and short life expectancy, individual preferences.

People whose GPs used a structured diabetes form were more likely to achieve the HbA1c and LDL cholesterol targets. GP usage of the form was also associated with higher odds of performing microvascular screening procedures (OR 2.65) [6].

Prescribing and intensifying medication is the GP’s main tool to influence risk factor control. Due to the cross-sectional design of the present study, we were not able to assess GP prescription patterns. GPs’ choices regarding prescriptions are best studied with longitudinal data. A review of GPs’ views on barriers to prescribing insulin found that time constraints, insulin skills, collaboration between primary and secondary care and perception of barriers for the person with diabetes influenced the initiation of insulin [20]. Another review found that delays in initiating or intensifying anti-hyperglycaemic therapy often exceeded 3 years [21]. Clinical inertia can be related to individuals with diabetes, their provider and healthcare system [22].

None of the included practice characteristics were significantly associated with the achievement of targets in the present study; however, with wide CIs we cannot exclude the possibility of some effects. A meta-analysis of RCTs showed no change in HbA1c where nurse prescribers supplemented a
team, however, in people served by nurse prescribers glycaemic control was non-inferior to people served by GPs [23]. In other studies significant and positive associations with diabetes specialized nurses, diabetes team, group education and reduced HbA1c have been reported [24,25]. Unfortunately, diabetes specialized nurses are rare in Norwegian general practice. Other studies have shown that multifaceted interventions on multidisciplinary teams resulted in better glycaemic control [26], and benchmarking in the multinational OPTIMISE study increased the number of people achieving blood pressure and LDL cholesterol targets [27].

We describe statistically significant variation in the proportion of people achieving targets among GPs within practices, and correspondingly, moderately sized median ORs and intraclass correlation coefficients. An intraclass correlation coefficient of 3% for clustering at practices was found for the combined achievement of HbA1c, blood pressure and cholesterol in a large study from general practice in UK [28]. Three-level studies on treatment targets in general practice are rare; however, one study showed that > 95% of the variance in HbA1c outcomes was at the population level, whereas only 2.8% and 1.9% was at the GP and practice level [11]. The variance pattern did not change when five population and three GP characteristics were added to the model. Their model explained 12% of the total variation; it was very similar to the presented full model [11,29,30]. We lack information on population characteristics regarding diet, physical activity, individual barriers, adherence to therapy, and comorbidities. We would also have liked to assess the effect of good GP communicators and dedicated prescribers, GPs with a special interest in diabetes, and GPs’ barriers to treatment.

The use of electronic health records as a data source can result in a considerable amount of missing data; however, in the present study all 9342 medical journals were manually scrutinized by research nurses who supplemented the database with information not captured electronically. Missing data were imputed, including missing measurements for HbA1c, blood pressure and LDL cholesterol values, which may protect against bias from data missing not at random [7].

In summary, the clinical management of diabetes is challenging, and only one in five people with diabetes met all three targets for HbA1c, blood pressure and LDL cholesterol. The largest variation in the achievement of targets was at the population level. However, the proportion of people reaching target varied among GPs and practices, also after adjusting for case mix. Most of the variation in risk factor control was not explained by the 12 population, 10 GP and four practice characteristics included in the present study. Despite this unexplained variation, the clinical implications of the study are that more attention should be focused on young people, people with obesity and those with macrovascular disease, and the use of a structured diabetes form is recommended.

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Competing interests

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Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1a. Characteristics of people with type 2 diabetes with adjusted predicted mean difference for the achievement of HbA1c, blood pressure or LDL cholesterol target.

Table S1b. Characteristics of general practitioners with adjusted predicted mean difference for the achievement of HbA1c, blood pressure or LDL cholesterol targets.

Table S1c. Characteristics of practices with adjusted predicted mean difference for the achievement of HbA1c, blood pressure or LDL cholesterol targets.

Table S2a. Characteristics of people with type 2 diabetes and adjusted predicted probabilities for the achievement of HbA1c, blood pressure or LDL-cholesterol targets.

Table S2b. Characteristics of general practitioners with adjusted predicted probabilities for the achievement of HbA1c, blood pressure or LDL cholesterol target.

Table S2c. Characteristics of practices with adjusted predicted probabilities for the achievement of HbA1c, blood pressure or LDL cholesterol target.

Table S3. Variation among general practitioners (n=281) and practices (n=77) in the achievement of HbA1c, blood pressure and LDL cholesterol treatment targets in 9342 people with type 2 diabetes.