Research: Epidemiology

Variation in prescribing of lipid-lowering medication in primary care is associated with incidence of cardiovascular disease and all-cause mortality in people with screen-detected diabetes: findings from the ADDITION-Denmark trial

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Abstract

Aims To examine variation between general practices in the prescription of lipid-lowering treatment to people with screen-detected Type 2 diabetes, and associations with practice and participant characteristics and risk of cardiovascular events and all-cause mortality.

Methods Observational cohort analysis of data from 1533 people with screen-detected Type 2 diabetes aged 40–69 years from the ADDITION-Denmark study. One hundred and seventy-four general practices were cluster randomized to receive: (1) routine diabetes care according to national guidelines (623 individuals), or (2) intensive multifactorial target-driven management (910 individuals). Multivariable logistic regression was used to quantify the association between the proportion of individuals in each practice who redeemed prescriptions for lipid-lowering medication in the two years following diabetes diagnosis and a composite cardiovascular disease (CVD) outcome, adjusting for age, sex, prevalent chronic disease, baseline CVD risk factors, smoking and lipid-lowering medication, and follow-up time.

Results The proportion of individuals treated with lipid-lowering medication varied widely between practices (0–100%). There were 118 CVD events over 9431 person-years of follow-up. For the whole trial cohort, the risk of CVD was significantly higher in practices in the lowest compared with the highest quartile for prescribing lipid-lowering medication [adjusted odds ratio (OR) 3.4, 95% confidence interval (CI) 1.6–7.3]. Similar trends were found for all-cause mortality.

Conclusions More frequent prescription of lipid-lowering treatment was associated with a lower incidence of CVD and all-cause mortality. Improved understanding of factors underlying practice variation in prescribing may enable more frequent use of lipid-lowering treatment. The results highlight the benefits of intensive treatment of people with screen-detected diabetes (Clinical Trials Registry No; NCT 00237549).

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Introduction

The cardioprotective benefits of lipid-lowering treatment are well established among people with clinically diagnosed diabetes. Lipid-lowering treatments are associated with a
What’s new

- Despite the well-established cardioprotective benefits of lipid-lowering treatment in Type 2 diabetes, evidence suggests large variations in statin use in primary care.
- Variation may be particularly high among people with screen-detected diabetes because general practitioners (GPs) might be reluctant to prescribe cardioprotective drugs for asymptomatic patients.
- There was wide variation in the prescription of lipid-lowering treatment among people with screen-detected diabetes in Danish primary care; more frequent prescription of lipid-lowering treatment was associated with a lower incidence of cardiovascular disease and all-cause mortality.
- More work is needed to improve understanding of the factors underlying practice variation in prescribing in order to encourage GPs to offer lipid-lowering treatment to this high-risk group.

Variations in lipid-lowering treatment may be particularly high among people with newly diagnosed diabetes. Research suggests that general practitioners (GPs) may be reluctant to prescribe cardioprotective drugs for asymptomatic patients [8], for whom the burden of treatment may seem greater than the burden of the disease [9]. Individuals detected earlier in the disease trajectory may, therefore, have reduced access to potentially beneficial treatment. With the advent of national screening programmes, a growing number of people will fall into this category.

The ADDITION study is a multi-centre cluster-randomized trial evaluating cardiovascular outcomes in people with screen-detected diabetes. Intensive treatment was associated with a non-significant 17% reduction in risk of cardiovascular events over five years in the intensive group [10]. In the Danish arm of the ADDITION study, we have access to information about individual participants’ redeemed prescriptions through the Danish National Prescription Registry. We aimed to characterize the variation in lipid-lowering treatment among people with screen-detected diabetes, and to examine associations with practice and participant characteristics as well as cardiovascular outcomes and all-cause mortality during 6.5 years of follow-up.

Participants and methods

Study design

ADDITION-Denmark consists of two phases, a pragmatic screening programme and a cluster-randomized trial comparing the effects of intensive multifactorial therapy with routine care among individuals with screen-detected Type 2 diabetes. Full details of the study are published elsewhere (Clinical Trials Registry No; NCT 00237549) [10]. Ethical approval was granted by the Region Midt Ethical Committee, Denmark. All participants provided informed consent.

In total, 175 practices (85 randomized to routine care and 90 randomized to intensive treatment) in five counties (Copenhagen, Aarhus, Ringkøbing, Ribe and South Jutland) carried out the screening programme and identified individuals with undiagnosed prevalent diabetes who were subsequently included in the treatment phase of the study. Population-based stepwise screening programmes among people aged 40–69 years without known diabetes, were undertaken between 2001 and 2006. In total, 163 185 individuals registered with participating practices were sent a validated risk score questionnaire [11] with an invitation to visit their family doctor for stepwise diabetes testing if they had a risk score ≥ 5 (maximum 15 points). The risk score was developed using the Danish Inter99 population. Sensitivity for predicting undiagnosed diabetes varied from 68.9 to 77.0%, and specificity from 68.8 to 78%, using four different cut-off points [11]. External validation using the chosen cut-point of ≥ 5 was completed using data from 1028 individuals in a pilot for the ADDITION study and revealed a sensitivity of 76.0% (95% confidence interval (CI): 58.3–90.3) and specificity of 72.2% (95% CI: 69.3–75.1) for diabetes. Individuals were diagnosed with diabetes according to 1999 WHO criteria and were subsequently managed according to the treatment regimen to which their practice was allocated: routine care or intensive treatment. General practitioners (GPs) assessed patients against exclusion criteria: an illness with a life expectancy of < 12 months, housebound, pregnancy or lactation, or psychological or psychiatric problems that were likely to invalidate informed consent. Overall, 1533 eligible participants with screen-detected diabetes agreed to take part.

Intervention

The characteristics of the interventions to promote intensive treatment have been described previously [10]. Further
details are available at the study website (http://www.addition.au.dk). We aimed to educate and support GPs, practice nurses and participants in target-driven management (using medication and promotion of healthy lifestyles) of hyperglycaemia, blood pressure and cholesterol, based on the stepwise regimen used in the Steno–2 study [12]. Targets included HbA1c < 53 mmol/mol (7.0%), blood pressure ≤ 135/85 mm Hg, cholesterol < 5 mmol/l without ischaemic heart disease or < 4.5 mmol/l with ischaemic heart disease, and prescription of aspirin to those treated with anti-hypertensive medication. In accordance with the Heart Protection Study [13], the treatment algorithm included a recommendation to prescribe a statin to all patients with a cholesterol level ≥ 3.5 mmol/l. GPs in the intensive treatment group were advised to start lipid-lowering treatment within four weeks of the diagnosis of diabetes. In the routine care group, participants received the standard pattern of diabetes care according to current recommendations [14].

**Measurement and endpoints**

Health assessments at baseline included biochemical and anthropometric measures and were undertaken by centrally trained staff following standard operating procedures. All biochemical measures were analysed in two regional laboratories. Standardized self-report questionnaires were used to collect information on lifestyle habits. We also collected relevant data from Danish national registries and linked information using the unique civil registration number. Prescription data were obtained from the Danish National Prescription Registry, which contains information on all prescription drugs redeemed at Danish community pharmacies. Lipid-lowering medication was defined as any ATC-group code C10. Data on education, income and cohabitation status were retrieved from Statistics Denmark. Education was categorized according to UNESCO’s *International Standard Classification of Education* [15]. Income was equivalence-weighted on the basis of the OECD-modified scale [16] in which the first adult in the household is given a weight of 1, the second adult is given a weight of 0.5 and each child is given a weight of 0.3. Cohabitation status was categorized into two groups: single and cohabiting. Information on prevalent chronic disease, including ischaemic heart disease (ICD–10 I20.0–25.9), stroke (ICD–10 I60.0–69.8) and cancer (ICD–10 C00.0–97.9), was retrieved from the Danish National Patient Registry, which covers all hospitalizations in Denmark.

Individuals were followed for a mean of 6.5 years. The primary outcome was time to first cardiovascular event after diagnosis of diabetes, including cardiovascular mortality, cardiovascular morbidity (non-fatal myocardial infarction and non-fatal stroke), revascularization and non-traumatic amputation. The secondary outcome was all-cause mortality. The Danish Civil Registration System and the Danish National Patient Register was searched on 31 December 2009 for deaths and for ICD–10 codes for cardiovascular events (I08–177), surgical procedures concerning amputations (chapters KNFQ, KNHQ, KNDQ, KNCQ) and revascularizations (chapters KF and KP of the NOMESCO Classification of Surgical Procedures. Sundhedsstyrelsen and Munksgaard, Copenhagen, 2005). All events were independently adjudicated by two members of a local endpoint steering committee according to an agreed protocol using standardized case report forms.

**Statistical analysis**

For each general practice, we calculated the proportion of individuals who redeemed at least three prescriptions of lipid-lowering medication within the first two years of diagnosis, of which the first was redeemed in the first year after diagnosis. These data were displayed in a ranked bar chart and divided into quartiles. Baseline practice and participant characteristics of the trial cohort were described by treatment group quartile. Practice screening intensity was calculated as the median number of patients in the target population who were screened for diabetes divided by the median number of participants in the target population. We compared practice and participant characteristics across quartiles using Kruskal–Wallis tests and chi-squared tests (where appropriate). Logistic regression was used to quantify the association between quartiles of proportions of individuals with screen-detected diabetes in practices who were prescribed lipid-lowering treatment and (1) risk of the composite CVD outcome and (2) risk of all-cause mortality among people with screen-detected diabetes. All models were adjusted for age, sex, previous ischaemic heart disease, previous stroke, previous cancer, prescription of lipid-lowering medication prior to diagnosis (according to the same definition used above), smoking, baseline values for HbA1c, total cholesterol, systolic blood pressure, diastolic blood pressure and BMI and follow-up time. Models were run in the whole trial cohort and separately by trial group. We also examined the same associations (with quartiles of prescribed medication) using a Cox proportional hazards model. We ran an individual participant level analysis exploring the association between lipid-lowering prescribing (yes/no) and CVD incidence, adjusting for the same confounders listed above and accounting for clustering by general practice. Sensitivity analyses were conducted to examine whether the overall result remained the same after excluding practices with only one or two participants. All data were analysed using Stata Version 12.0 (STATA Corp., College Station, TX, USA).

**Results**

One GP practice with four participants was excluded due to missing information on GP characteristics. We subsequently excluded 20 individuals who experienced a CVD endpoint or died in the first two years of follow-up. Table 1 shows
| Characteristics | Treatment intensity | Quartile 1 (highest) | Quartile 2 | Quartile 3 | Quartile 4 (lowest) | P-value* |
|-----------------|---------------------|----------------------|------------|-----------|---------------------|---------|
| **Practice**    |                     |                      |            |           |                     |         |
| Number          |                     | 42                   | 45         | 43        | 44                  | 0.174   |
| Median number of patients per practice in the target population (IQR) (A) | 656 (555–901) | 888 (598–1456) | 728 (522–1224) | 720 (618–956) |
| Prescribed lipid-lowering medication, % (range) | N/A | Whole trial cohort | 86.7 (73.3–100) | 56.0 (40.9–69.2) | 30.0 (21.1–40.0) | 6.2 (0–20) |
| Routine care    |                     | 87.8 (76.9–100)      | 68.7 (54.3–76.5) | 36.4 (21.1–50.0) | 5.8 (0–20) |
| Median number of ADDITION trial participants per practice (IQR) | 6 (3–12) | 10 (6–16) | 7 (4–13) | 5 (2–7.5) | < 0.001 |
| Median number of patients in the target population screened per practice (IQR) (B) | 151 (91–196) | 157 (111–211) | 146 (89–192) | 120 (86–166) |
| Screening intensity (B/A) (%) | 20.7 | | 18.9 | 17.4 | 16.4 | 0.034 |
| Median number of GPs per practice (range) | 1 (1–5) | 1 (1–6) | 1 (1–6) | 1 (1–4) |
| **Participants** |                     |                      |            |           |                     |         |
| Number          |                     | 328                  | 550        | 387       | 244 |
| Mean age at diagnosis (SD), years | 59.6 (3.5) | 59.7 (2.9) | 59.6 (2.7) | 58.8 (5.0) |
| Men, %          |                     | 53.4                 | 57.1       | 53.8      | 66.0 |
| Education       |                     |                      |            |           |                     |         |
| > 15 years, n (%) | 43 (13.4) | 84 (15.4) | 55 (14.6) | 31 (12.9) |
| 10–15 years, n (%) | 159 (49.4) | 256 (47.1) | 180 (47.8) | 113 (46.9) |
| < 10 years, n (%) | 120 (37.3) | 204 (37.5) | 142 (37.7) | 97 (40.3) |
| Income          |                     |                      |            |           |                     |         |
| > 80 percentile, n (%) | 67 (20.4) | 112 (20.4) | 75 (19.4) | 48 (19.7) |
| 20–80 percentiles, n (%) | 197 (60.1) | 331 (60.2) | 229 (59.2) | 142 (58.2) |
| < 20 percentile, n (%) | 64 (19.5) | 107 (19.5) | 83 (21.5) | 54 (22.1) |
| Cohabiting (%) |                     | 66.7                 | 72.9       | 67.1      | 69.8 |
| Mean BMI (SD), kg/m² | 30.9 (2.9) | 31.2 (1.8) | 31.4 (2.2) | 31.2 (3.2) |
| Current smoker (%) | 31.1 | | 32.3 | 45.5 | 26.3 | 0.001 |
| Prevalent ischaemic heart disease (%) | 11.1 | | 10.4 | 8.1 | 3.0 | 0.004 |
| Prevalent stroke (%) | 3.2 | | 2.3 | 3.9 | 1.2 | 0.127 |
| Prevalent cancer (%) | 2.5 | | 4.4 | 5.7 | 1.5 | 0.014 |
| Charlson comorbidity index ≥ 1 (%) | 13.0 | | 12.5 | 11.2 | 9.9 | 0.718 |
| Mean HbA₁c, mmol/mol | 48.6 | | 49.7 | 51.9 | 50.8 | 0.112 |
| Mean HbA₁c (SD), % | 6.6 (0.7) | 6.7 (0.6) | 6.9 (0.5) | 6.8 (1.1) |
| Mean total cholesterol (SD), mmol/l | 5.5 (0.6) | 5.6 (0.4) | 5.7 (0.3) | 5.5 (0.7) |
| Mean systolic blood pressure (SD), mmHg | 141.4 (7.3) | 144.8 (8.1) | 144.7 (9.7) | 146.6 (14.9) |
| Mean diastolic blood pressure (SD), mmHg | 84.3 (5.5) | 85.7 (4.3) | 85.9 (4.0) | 86.7 (6.4) |
| Modelled CVD risk ≥ 5 points (%)** | 50.6 | | 59.0 | 60.5 | 61.3 | 0.191 |
| Number of CVD events, n (%) | 14 (4.3) | | 38 (6.9) | 42 (10.9) | 24 (9.8) | 0.005 |
| All-cause mortality, n (%) | 30 (9.1) | | 46 (8.4) | 33 (8.5) | 21 (8.6) | 0.983 |
| Median person-years of follow-up (IQR) | 6.1 (4.0–7.0) | | 6.4 (5.8–6.8) | 6.7 (6.0–7.5) | 7.5 (6.4–7.9) | < 0.001 |

*For group differences from the Kruskal-Wallis equality-of-populations rank test, chi-squared test or ANOVA test.
**Modelled CVD risk was computed using the SCORE model.
baseline practice \((n = 174)\) and participant \((n = 1509)\) characteristics by quartile of lipid-lowering treatment. The mean (SD) age was 59.6 (6.9) years; 57% were male and the mean BMI was 31.2 kg/m². The median [interquartile range (IQR)] number of participants per practice in the target population was 720 (584–1070).

**Treatment variation**

Figure 1 shows the proportion of participants who redeemed lipid-lowering medication within the first two years of diagnosis in each GP practice. Proportions varied widely from 0% to 100% in both study groups. However, lipid-lowering treatment was prescribed significantly more frequently in the intensive treatment group than the routine care group [intensive treatment: median (IQR): 64.7% (33.3–75.0); routine care: 33.3% (23.1–50.0), \(P < 0.001\)].

**Practice- and participant-level factors associated with variation**

Compared with practices with low levels of prescribing of lipid-lowering medication, higher prescribing practices had screened more of their eligible population and had greater numbers of people with screen-detected diabetes (Table 1). Practices were similar for all other examined characteristics.

Participant characteristics were similar across the treatment quartiles for most socio-demographic and clinical characteristics (Table 1). Compared with individuals in the bottom quartile for lipid-lowering prescribing, those in the top quartile were more likely to have a history of ischaemic heart disease.

**Association between treatment variation and CVD events**

One hundred and eighteen people experienced a CVD event (8%) over 9431 person-years of follow-up, with the highest number of events in the practices who prescribed lipid-lowering medication to the fewest individuals. Table 2 shows the crude and adjusted ORs for the association between quartiles of proportion of people prescribed lipid-lowering treatment in practices and risk of CVD events. When examining the whole trial cohort, the risk of CVD was significantly higher in practices in the lowest quartile compared with the highest quartile for prescribing of lipid-lowering medication (adjusted OR 3.4, 95% CI 1.6–7.3). The association between lipid-lowering prescribing and CVD events was stronger in the routine care than the intensive treatment group; the odds of CVD increased as the prescription of lipid-lowering medication decreased. There was a significant trend in OR over the four quartiles \((P < 0.001)\).

**Association between treatment variation and all-cause mortality**

One hundred and thirty participants died over 6.5 years of follow-up. When examining the whole trial cohort, all-cause mortality was significantly higher in practices in the lowest quartile compared with the highest quartile for prescribing of lipid-lowering medication (adjusted OR 2.9, 95% CI 1.1–
Table 2  Crude and adjusted odds ratios for the association between lipid-lowering treatment group, a composite CVD endpoint and all-cause mortality by trial group in ADDED-Denmark

| Groups of lipid-lowering treatment | Mean proportion prescribed lipid-lowering treatment (range) | Crude OR for incident CVD (95% CI) | Adjusted* OR for incident CVD (95% CI) | Crude OR for all-cause mortality (95% CI) | Adjusted OR for all-cause mortality (95% CI)* |
|-----------------------------------|----------------------------------------------------------|-----------------------------------|----------------------------------------|------------------------------------------|---------------------------------------------|
| Overall Cohort                    |                                                          |                                   |                                        |                                          |                                             |
| 1 (comparison)                    | 86.7 (73.3–100)                                          | 1                                 | 1                                      | 1.9 (1.0–3.8)                            | 1.4 (0.6–3.3)                              |
| 2                                 | 56.0 (40.9–69.2)                                          | 1.7 (0.9–3.0)                     | 3.2 (1.5–6.7)                          | 0.9 (0.5–1.5)                            | 1.6 (0.7–3.8)                              |
| 3                                 | 30.0 (21.1–40.0)                                          | 2.7 (1.5–5.1)                     | 3.4 (1.6–7.3)                          | 0.9 (0.5–1.6)                            | 2.9 (1.1–7.8)                              |
| 4                                 | 6.2 (0–20.0)                                              | 2.4 (1.3–4.6)                     |                                        |                                          |                                             |
| Intensive Treatment Group         |                                                          |                                    |                                        |                                          |                                             |
| 1 (comparison)                    | 87.8 (76.9–100)                                          | 2                                 | 2                                      | 2.8 (1.3–6.9)                            | 1.4 (0.8–2.6)                              |
| 2                                 | 68.7 (54.3–76.5)                                          | 2.2 (1.0–4.8)                     | 3.2 (1.1–9.1)                          | 1.3 (0.7–2.5)                            | 4.5 (1.2–15.9)                             |
| 3                                 | 36.4 (21.1–50.0)                                          | 2.9 (1.2–6.7)                     | 2.8 (1.0–7.9)                          | 0.6 (0.2–1.5)                            | 1.8 (0.5–7.0)                              |
| 4                                 | 5.8 (0–20.0)                                              | 1.9 (0.7–4.7)                     |                                        |                                          |                                             |
| Routine Care Group                |                                                          |                                    |                                        |                                          |                                             |
| 1 (comparison)                    | 79.7 (57.1–100)                                          | 1                                 | 1                                      | 0.7 (0.2–2.0)                            | 1.3 (0.3–4.8)                              |
| 2                                 | 45.3 (35.0–53.8)                                          | 0.5 (0.2–1.4)                     | 4.7 (1.8–12.2)                        | 1.4 (0.5–3.4)                            | 3.2 (1.0–9.9)                              |
| 3                                 | 28.3 (21.1–33.3)                                          | 2.6 (1.1–6.1)                     | 4.7 (1.8–14.0)                        | 1.8 (0.8–4.3)                            | 7.3 (2.0–26.7)                             |
| 4                                 | 6.5 (0–20.0)                                              | 2.2 (0.9–5.5)                     |                                        |                                          |                                             |

OR, odds ratio.  
*OR adjusted for age, sex, prevalent ischaemic heart disease, stroke and cancer, use of lipid-lowering drugs before screening, smoking, Hba1c, total cholesterol, systolic blood pressure, diastolic blood pressure, BMI and follow-up time.

Discussion

We observed a large variation in the prescribing of lipid-lowering treatment within the first four weeks of a diagnosis of diabetes. The variation did not appear to be explained by participant levels of modifiable cardiovascular risk factors and follow-up time. There was an association between prescription of lipid-lowering treatment and all-cause mortality, but not CVD events, at the individual level. There was no association between treatment variation and all-cause mortality in either trial using Cox regression and all-cause mortality in either trial being direction of effect. In an individual participant-level analysis, all-cause mortality was significantly lower among individuals prescribed lipid-lowering treatment compared with those who were not (adjusted OR 0.58; 95% CI 0.35–0.97). There was no association between lipid-lowering treatment and CVD events at the whole trial cohort, but not in the routine care and intensive treatment groups. Similar trends were observed in the routine care and the intensive treatment groups.

Sensitivity analyses

When using Cox regression there was a significant association between treatment variation and CVD events in the routine care group, even among GPs in intensive treatment groups when analysed separately. There was no significant association between treatment variation and all-cause mortality in either trial using Cox regression and all-cause mortality in either trial being direction of effect. In an individual participant-level analysis, all-cause mortality was significantly lower among individuals prescribed lipid-lowering treatment compared with those who were not (adjusted OR 0.58; 95% CI 0.35–0.97). There was no association between lipid-lowering treatment and CVD events at the whole trial cohort, but not in the routine care and intensive treatment groups.
Previous research suggests that the prescribing behaviour of doctors is likely to be the biggest factor contributing to the variation in statin prescribing for CVD prevention in primary care [4–7]. Qualitative research shows that GPs face a variety of barriers to initiating statin treatment and instigating CVD prevention more generally. These include differing treatment targets and difficulties in prioritizing patients for treatment and in interpreting primary prevention risk assessment tools [4,22,23]. There are also fears about cost, increased workload, and adherence to treatment, as well as concerns about medicalization and adverse effects on patient health behaviours [4]. The results from our study should also be considered in light of national interest and uncertainty about screening and early treatment for diabetes in Denmark. Articles in the national and international press have suggested that diabetes screening is unnecessary and that the health system is over-medicalizing its citizens [24–27]. These factors may have contributed to GPs being reluctant to prescribe lipid-lowering treatments to asymptomatic patients at an early stage in the course of the disease, and to patients being reluctant to redeem such prescriptions [28]. Future work might collect data on a wider range of potential determinants of prescribing to investigate this issue in more detail. It may also be useful to compare our results with countries like the UK who have a direct financial incentive to prescribing.

Strengths and limitations

Participants were recruited from a large, representative, population-based sample from five different counties in Denmark. There was 99.9% endpoint ascertainment and all CVD events were independently adjudicated. Prescription data were obtained from the Danish National Prescription Registry, which captures all prescription drugs dispensed at community pharmacies. We were able to adjust for a wide range of potential confounders, using information collected from participants at their baseline visit and data retrieved from Statistics Denmark and the Danish National Patient Registry.

In terms of limitations, this was a post-hoc research question using observational data from a trial cohort. Adjustment for age, sex, prevalent chronic disease, baseline cardiovascular risk factors and follow-up time did not alter the association between treatment variation and incident CVD. This makes it unlikely that participant-level comorbidity and differences in follow-up time confounded the observed association and that general-practice-level factors are most likely responsible for the variation in treatment. However, we cannot rule out the possibility of confounding by intention, e.g. practices prescribing more lipid-lowering medication may also encourage more lifestyle changes and prescribe more nicotine replacements, anti-hypertensive and glucose-lowering medication, which may also be linked to the outcomes. Although we showed that higher prescribing practices had screened more of their eligible population and had greater numbers of participants with screen-detected diabetes, we were not able to examine the importance of other general practice factors such as: the age and gender of GPs, the number of GPs per practice and number of other healthcare providers per practice. The recruitment of general practices was not random, potentially limiting the generalizability of our results. However, we covered a large geographical area and participating practices were nationally representative for key characteristics [10]. We do not have data on individuals who were prescribed lipid-lowering medication but chose not to pick it up at their community pharmacy. However, evidence from a trial nested within ADDITION-Denmark suggests that compliance rates were very high (close to 100%) [29]. Given that individuals who do not redeem their prescriptions are more likely be to those with higher HbA1c values and complications of diabetes [30], this might have led to an under-estimation of the inverse association between prescribing lipid-lowering medication and incident CVD. We could not ascertain whether the low proportions of participants prescribed lipid-lowering treatments in some practices might be due to individuals being started on lipid-lowering treatment but experiencing side effects and then stopping them.

Conclusion

We found a wide variation between practices in the prescription of lipid-lowering treatment among individuals with screen-detected diabetes and demonstrated a significant association between the frequency of lipid-lowering treatment and CVD and all-cause mortality – both being favourably influenced by more frequent treatment. More work is needed to improve understanding of the factors
underlying practice variation in prescribing in order to encourage GPs to offer lipid-lowering treatment and other preventive interventions to this high-risk group. These results lend support to the benefits of treatment early in the course of the disease. In tailoring treatment decisions to individuals with screen-detected Type 2 diabetes, consideration should be given to the possibilities of both over- and under-treatment.

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Competing interests

RKS, AHC, KB-J, MC, AS and JSC declare no support from any organization for the submitted work; no financial relationships with any organizations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work. SJG received an honorarium and reimbursement of travel expenses associated with membership of an independent data-monitoring committee for a randomized trial of a medication to lower glucose; he received a fee for chairing an educational meeting for a qualitative study on barriers to the use of statins and the implementation of coronary heart disease prevention in primary care. TL reports grants from National Health Services, grants from Strategic Research, the Danish Research Foundation for General Practice, grants from Novo Nordisk Foundation, grants from The Danish Centre for Evaluation and Health Technology Assessment, grants from the Diabetes Fund of the National Board of Health, grants from The Danish Medical Research Council, grants from the Aarhus University Research Foundation, grants from Novo Nordisk AS, Novo Nordisk Scandinavia AB, Novo Nordisk UK, Astra Denmark, Pfizer Denmark, GlaxoSmithKline Pharma Denmark, Servier Denmark A/S and HemoCue Denmark A/S, during the conduct of the study; other from Shares in Novo Nordisk, outside the submitted work.

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