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Prevalence of macrovascular disease amongst type 2 diabetic patients detected by targeted screening and patients newly diagnosed in general practice: the Hoorn Screening Study

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Abstract. Spijkerman AMW, Henry RMA, Dekker JM, Nijpels G, Kostense PJ, Kors JA, Ruwaard D, Stehouwer CDA, Bouter LM, Heine RJ. (VU University Medical Center, Amsterdam and Erasmus University Medical Center, Rotterdam, The Netherlands; and Royal Netherlands Embassy, Washington, DC, USA). Prevalence of macrovascular disease amongst type 2 diabetic patients detected by targeted screening and patients newly diagnosed in general practice: the Hoorn Screening Study. *J Intern Med* 2004; **256**: 429–436.

Objectives. Screening for type 2 diabetes has been recommended and targeted screening might be an efficient way to screen. The aim was to investigate whether diabetic patients identified by a targeted screening procedure differ from newly diagnosed diabetic patients in general practice with regard to the prevalence of macrovascular complications.

Design. Cross-sectional population-based study.

Setting. Population study, primary care.

Subjects. Diabetic patients identified by a population-based targeted screening procedure (SDM patients), consisting of a screening questionnaire and a fasting capillary glucose measurement followed by diagnostic testing, were compared with newly diagnosed diabetic patients in general practice (GPDM patients).

Ischaemic heart disease and prior myocardial infarction were assessed by ECG recording. Peripheral arterial disease was assessed by the ankle-arm index. Intima-media thickness of the right common carotid artery was measured with ultrasound.

Results. A total of 195 SDM patients and 60 GPDM patients participated in the medical examination. The prevalence of MI was 13.3% (95% CI 9.3–18.8%) and 3.4% (1.0–11.7%) in SDM patients and GPDM patients respectively. The prevalence of ischaemic heart disease was 39.5% (95% CI 32.9–46.5%) in SDM patients and 24.1% (15.0–36.5%) in GPDM patients. The prevalence of peripheral arterial disease was similar in both groups: 10.6% (95% CI 6.9–15.9%) and 10.2% (4.7–20.5%) respectively. Mean intima-media thickness was 0.85 mm (± 0.17) in SDM patients and 0.90 mm (± 0.20) in GPDM patients. The difference in intima-media thickness was not statistically significant.

Conclusions. Targeted screening identified patients with a prevalence of macrovascular complications similar to that of patients detected in general practice, but with a lower degree of hyperglycaemia.

Keywords: cardiovascular disease, early diagnosis, epidemiology, macrovascular complications, screening, type 2 diabetes.

Introduction

Type 2 diabetes is a common and serious disease. People with type 2 diabetes have a two to fourfold higher risk of cardiovascular mortality, compared with people who do not have diabetes [1]. The fact that this higher risk is already present in newly diagnosed diabetic patients has been shown in population-based studies [2, 3]. Several of these studies have also shown that the prevalence of macrovascular disease in newly diagnosed diabetic patients is intermediate between the prevalence in previously diagnosed diabetic patients and the prevalence in individuals with normal glucose tolerance [4–6]. The presence of diabetic complications at the time of clinical diagnosis is one of the reasons why screening is recommended for type 2 diabetes [7]. Screening is directed at the identification of diabetic patients at an early stage of the disease, when there are few complications, if any. Universal screening implies screening every person in the entire population. The performance of an oral glucose tolerance test (OGTT) or a fasting or random glucose measurement in the entire study population, as has been the case in population-based studies of glucose intolerance, can be considered as universal screening.

Targeted screening seems to be a more practical and efficient way of screening. In this type of screening a high-risk population is first selected by a questionnaire or a risk score and the performance of the 'invasive', and in case of an OGTT, time-consuming, diagnostic test is restricted to this high-risk population. However, targeted screening studies to date have only focused on the yield of the screening procedure, and none have yet described the prevalence of macrovascular complications in diabetic patients identified by targeted screening [8–10]. In particular, it is unclear to what extent these diabetic patients differ from newly diagnosed diabetic patients in general practice. With screening one would expect to identify patients earlier and with a lower prevalence of complications. In view of these considerations, we compared the prevalence of ECG abnormalities and peripheral arterial disease and the mean carotid intima-media thickness in diabetic patients detected by targeted screening and newly diagnosed diabetic patients in general practice. This study was based on a population-based targeted screening procedure that consisted of a

screening questionnaire [11] and a fasting capillary whole blood glucose measurement followed by diagnostic testing (OGTT) in high-risk individuals [12].

Material and methods

Study population

Diabetic patients detected by targeted screening. The targeted screening procedure was carried out from 1998 to 2000 in the West-Friesland region of the Netherlands, amongst 11 679 inhabitants aged 50–75 years, as described previously [12]. Briefly, the first step of the screening procedure consisted of the Symptom Risk Questionnaire (SRQ), which includes questions about age, sex, body mass index (BMI), family history of diabetes, use of antihypertensive medication, frequent thirst, shortness of breath, claudication, and use of a bicycle for transportation [11]. The SRQ was developed in the Hoorn Study to identify people at increased risk of having undiagnosed type 2 diabetes [11]. The SRQ was validated against the 1999 WHO diagnostic criteria of diabetes in a separate random sample of the population of Hoorn. The sensitivity, specificity, positive and negative predictive value of an SRQ score of 6 are 66, 70, 13 and 97% respectively (A. M. W. Spijkerman, unpublished data). Participants with an SRQ score ≤ 6 were considered to be at low risk for undiagnosed diabetes, and were therefore not invited to participate in any further testing. For individuals with an SRQ score > 6 , the second step of the screening was a fasting capillary whole blood glucose measurement. In all individuals with a capillary whole blood glucose level > 5.5 and ≤ 8.5 mmol L⁻¹, a venous sample was drawn on the same occasion, and a 75 g OGTT was performed within 2 weeks. Participants with a capillary whole blood glucose of > 8.5 did not have an OGTT because their fasting levels were considered too high. Therefore, a fasting venous sample was drawn on two different occasions and diagnosis was based on two fasting plasma glucose measurements. The 1999 WHO diagnostic criteria for diabetes were applied: fasting plasma glucose of ≥ 7.0 mmol L⁻¹ on two separate occasions, or a 2-h plasma glucose level of ≥ 11.1 mmol L⁻¹ [13]. The total response for the invitation to the screening was 78% and the SRQ was calculated for 7736 participants, after exclusion of 741 nonparticipants,

417 previously diagnosed diabetic patients and 275 people with missing data or missing informed consent. A total of 3301 participants had an SRQ >6 and the response rates for the capillary blood glucose measurement and OGTT were 87 and 89% respectively. Amongst the participants of the OGTT, 216 had impaired glucose metabolism. The non-participants of the SRQ were significantly younger than participants and more likely to be men. The nonresponders for the OGTT were older than people who did participate. In total, 217 previously undiagnosed diabetic patients were identified in the targeted screening [12].

Diabetic patients newly diagnosed in general practice. All diabetic patients, aged 50–75 years, who were newly diagnosed from 1999 to 2001 in general practice in the towns of Den Helder and Medemblik (situated to the north of the West-Friesland region) were invited to participate in the study. For people without symptoms of hyperglycaemia, a fasting capillary glucose measurement of $\geq 6.1 \text{ mmol L}^{-1}$ or fasting plasma glucose of $\geq 7.0 \text{ mmol L}^{-1}$ on two separate occasions were the criteria for a diagnosis of diabetes. For individuals with symptoms of hyperglycaemia, (thirst, fatigue, frequent urination), one fasting capillary glucose measurement of $\geq 6.1 \text{ mmol L}^{-1}$ or one fasting plasma glucose of $\geq 7.0 \text{ mmol L}^{-1}$ was sufficient for a diagnosis of diabetes, according to the guidelines of the Dutch College of General Practice [14]. These diagnostic cut-off points are in accordance with the 1999 WHO diagnostic fasting criteria for diabetes. The general practitioners identified a total of 81 newly diagnosed diabetic patients. Of these, 10 were too young to participate in the present study (<50 years). As a result, 71 newly diagnosed diabetic patients were eligible and were invited consecutively to participate in the study. Ascertainment of referral of all newly diagnosed diabetic patients was not possible, because of Dutch privacy legislation.

Individuals with screening-detected type 2 diabetes (SDM) and all newly diagnosed diabetic patients in general practice (GPDM) were invited to undergo an extensive medical examination, including assessment of macrovascular complications.

Screening, diagnostic tests and physical examination were carried out in a standardized manner by trained PhD students and research assistants at the

Diabetes Research Center in Hoorn. All participants gave written informed consent. The Ethics Committee of the VU University Medical Center approved the study.

Measurements. Capillary fasting whole blood glucose levels were obtained with a Hemocue Blood Glucose Analyzer, based on the glucose-dehydrogenase method (Hemocue Nederland, Oosterwijk, the Netherlands). Plasma glucose concentrations were assessed by means of a glucose hexokinase method (Roche Diagnostics GmbH, Mannheim, Germany). HbA1c was determined by ion-exchange high-performance liquid chromatography with a Modular Diabetes Monitoring System (Bio-Rad, Veenendaal, the Netherlands). Serum total cholesterol, HDL cholesterol and triglycerides were measured by means of enzymatic techniques (Boehringer-Mannheim, Mannheim, Germany). The Friedewald formula was used to calculate LDL cholesterol, except if the triglyceride level was $>4.5 \text{ mmol L}^{-1}$, then LDL cholesterol was considered missing ($n = 5$ amongst SDM, $n = 1$ GPDM). High cholesterol was defined as serum total cholesterol $\geq 5.0 \text{ mmol L}^{-1}$, and high LDL cholesterol was defined as LDL-cholesterol $\geq 3.0 \text{ mmol L}^{-1}$. Dyslipidaemia was considered present when HDL cholesterol was $\leq 1.0 \text{ mmol L}^{-1}$ in men or ≤ 1.1 in women and triglyceride was $\geq 2.0 \text{ mmol L}^{-1}$ [15]. The albumin-to-creatinine ratio (ACR) was calculated to determine the presence of microalbuminuria. Urinary albumin was measured by means of rate nephelometry (Array Protein System, Beckman, Galway, Ireland). Urinary creatinine was measured by means of a modified Jaffé method. Subjects were classified as having (micro)albuminuria if they had an ACR of $>2.0 \text{ mg mmol}^{-1}$ [16].

Information about smoking habits and medication use was assessed by means of a questionnaire. Weight, height, and hip and waist circumferences were measured with subjects barefoot, wearing light clothes only. Blood pressure was calculated as the mean of two measurements, performed in a sitting position after 5 min of rest, with a random-zero sphygmomanometer (Hawksley-Gelman, Lancing, Sussex, UK). Overweight was defined as BMI $\geq 25 \text{ kg m}^{-2}$. Individuals were considered to be hypertensive if they had a diastolic blood pressure $\geq 90 \text{ mmHg}$, and/or a systolic blood pressure $\geq 140 \text{ mmHg}$, and/or they were taking antihypertensive medication [17].

Macrovascular complications. Standard 12-lead ECGs were recorded (CardioControl, Delft, The Netherlands) and coded according to the Minnesota code with an automated diagnostic classification system [Modular ECG Analysis System (MEANS)] [18, 19]. Prior myocardial infarction was defined as the presence of Minnesota codes 1-1 or 1-2 on the ECG-recording. Ischaemic heart disease was considered to be present with Minnesota codes 1-1, 1-2, 1-3, 4-1, 4-2, 4-3, 5-1, 5-2, 5-3 or 7-1 on the ECG-recording.

Doppler-assisted systolic blood pressure measurements were made in duplicate from the brachial, posterior tibial and dorsalis pedis arteries on both sides. The average pressure was calculated for the posterior tibial and dorsalis pedis arteries in each leg. The highest of these average pressure levels was used to calculate the ankle-arm index for each leg. Peripheral artery disease was defined as the presence of ankle-arm index <0.90 in either leg. An ankle-arm index of >1.50 (which possibly reflects medial arterial calcification [20]) was not observed in any of the participants.

Intima-media thickness of the right common carotid artery was obtained with the use of an ultrasound scanner equipped with a 7.5 MHz linear array probe (Pie 350 Series; Pie Medical BV, Maastricht, The Netherlands). The ultrasound scanner was connected to a personal computer equipped with vessel wall movement detection software and an acquisition system (Wall Track System 2; Pie Medical BV). This integrated set-up makes it possible to measure intima-media thickness, as described in detail elsewhere [21, 22]. Briefly, the carotid artery was visualized in B-mode, and an M-line perpendicular to the artery was positioned 10 mm proximal to the carotid bulb. After switching to M-mode, data acquisition in a real-time A-mode presentation on the computer screen was possible after trackball-assisted identification of the lumen of the artery. Ultrasound data were obtained during three consecutive measurements, each consisting of a 4-s period, triggered by the R-top of a simultaneously recorded ECG. Intima-media thickness of the posterior carotid wall was defined as the distance from the leading edge interface between lumen and intima to the leading edge interface between media and adventitia, automatically calculated from digitized cumulative radio frequency signals. The mean

intima-media thickness of the three measurements was used in the analyses.

Statistical analyses

The characteristics of SDM and GPDM patients were stratified for sex because of the well-known difference in cardiovascular risk factors between men and women. The characteristics of SDM and GPDM patients were compared, using Student's *t*-test for continuous variables, the chi-square test for dichotomous variables and the Mann-Whitney *U*-test for skewed variables. Fasting plasma glucose, HbA1c and triglyceride were presented as median and interquartile range because of their skewed distribution. Confidence intervals were calculated with CONFIDENCE INTERVAL ANALYSIS software, version 2.0 [23]. *P*-values were based on two-sided tests, and considered to be statistically significant if less than 0.05.

Results

In total, 195 of the 217 screening-detected diabetic patients participated in the assessment of macrovascular complications. The general practitioners identified a total of 71 newly diagnosed diabetic patients. Of these, eight declined participation in the study and three did not participate in the assessment of macrovascular complications. As a result, a total of 195 SDM and 60 GPDM patients underwent the extensive physical examination. Nonparticipants in the medical examination tended to be older in both groups, but this difference was not statistically significant. There were no differences between participants and nonparticipants in the physical examination in either group with respect to sex and glucose levels (data not shown). In the SDM group, data were complete for 195, 180 and 165 patients for ECGs, peripheral arterial disease and intima-media thickness respectively. In the GPDM group, two ECGs were missing, data on peripheral arterial disease were complete for 59 patients and intima-media thickness measurements were obtained from 51 patients. Patients with missing intima-media thickness data were more obese in both groups.

Table 1 shows the baseline characteristics of diabetic patients identified by screening and in general practice, stratified according to sex. The SDM patients were older than the GPDM patients,

Table 1 Baseline characteristics of diabetic patients identified by targeted screening and in general practice stratified according to sex

	Women		Men	
	SDM (n = 94)	GPDM (n = 30)	SDM (n = 101)	GPDM (n = 30)
Age (years)	65.3 (6.1)	62.3 (7.4)*	61.5 (7.4)	60.4 (6.7)
Fasting plasma glucose (mmol L ⁻¹)	7.9 (7.3–8.9)	8.7 (7.7–9.8)	7.8 (7.3–9.1)	9.3 (7.5–12.2)*
HbA1c (%)	6.4 (5.8–7.1)	8.1 (7.4–11.3)*	6.3 (5.7–7.1)	8.7 (7.4–10.7)*
Cholesterol (mmol L ⁻¹)	5.9 (1.1)	5.7 (0.9)	5.5 (1.1)	5.3 (1.1)
High cholesterol (%)	79.8	79.3	66.7	53.3
LDL cholesterol (mmol L ⁻¹)	3.64 (0.94)	3.56 (0.88)	3.50 (0.98)	3.44 (1.05)
High LDL cholesterol (%)	81.7	75.9	72.9	62.1
HDL cholesterol (mmol L ⁻¹)	1.4 (0.4)	1.2 (0.3)*	1.1 (0.2)	1.1 (0.4)
Triglycerides (mmol L ⁻¹)	1.7 (1.2–2.4)	1.9 (1.7–2.6)	1.7 (1.2–2.4)	1.6 (1.3–2.1)
Dyslipidaemia (%)	18.1	20.7	23.2	23.3
Lipid-lowering medication (%)	18.1	16.7	21.8	16.7
BMI (kg m ⁻²)	30.1 (6.2)	31.1 (6.3)	29.5 (4.4)	27.6 (4.6)*
Overweight (%)	85.1	86.7	92.1	62.1*
Waist-hip ratio	0.92 (0.08)	0.92 (0.07)	1.01 (0.06)	1.00 (0.07)
Systolic blood pressure (mmHg)	143 (20)	140 (25)	140 (16)	143 (21)
Diastolic blood pressure (mmHg)	86 (10)	82 (12)	85 (9)	85 (11)
Hypertension (%)	80.9	70.0	70.3	46.7*
Antihypertensive medication (%)	56.4	56.7	37.6	23.3
Microalbuminuria (%)	17.2	23.3	17.2	30.0
Current smoking (%)	11.7	26.7*	18.8	36.7*

Data are presented as mean (SD), median (interquartile range, IQR) or percentages. SDM screening detected diabetes mellitus, GPDM diabetes mellitus newly diagnosed in general practice. High cholesterol was defined as serum total cholesterol ≥ 5.0 mmol L⁻¹ and high LDL cholesterol as LDL cholesterol ≥ 3.0 mmol L⁻¹. Dyslipidaemia was considered present when HDL cholesterol was ≤ 1.0 mmol L⁻¹ in men or ≤ 1.1 in women and triglyceride was ≥ 2.0 mmol L⁻¹. BMI, body mass index, overweight was defined as BMI ≥ 25 . Hypertension was defined as diastolic blood pressure ≥ 90 mmHg, systolic blood pressure ≥ 140 mmHg, or use of antihypertensive medication, microalbuminuria as an albumin-to-creatinine ratio > 2.0 . *Significantly different from SDM ($P < 0.05$).

reaching statistical significance only in women. Glucose and HbA1c were higher in GPDM patients than in SDM patients, but the difference in glucose was not statistically significant in women. HDL

cholesterol was significantly lower in the GPDM women, but the prevalence of lipid abnormalities was similar in both groups and both sexes. In women, the prevalence of obesity was similar in

Table 2 Prevalence of macrovascular complications at the time of diagnosis in diabetic patients identified by targeted screening and in general practice

	SDM	GPDM
All participants		
Myocardial infarction (%)	13.3 (9.3–18.8)	3.4 (1.0–11.7)*
Ischaemic heart disease (%)	39.5 (32.9–46.5)	24.1 (15.0–36.5)*
Peripheral arterial disease (%)	10.6 (6.9–15.9)	10.2 (4.7–20.5)
Intima-media thickness (mm)	0.85 (0.17)	0.90 (0.20)
Women		
Myocardial infarction (%)	13.8 (8.3–22.2)	3.4 (0.6–17.2)
Ischaemic heart disease (%)	46.8 (37.0–56.8)	24.1 (12.2–42.1)*
Peripheral arterial disease (%)	8.1 (4.0–15.9)	6.7 (1.8–21.3)
Intima-media thickness (mm)	0.86 (0.14)	0.83 (0.18)
Men		
Myocardial infarction (%)	12.9 (7.7–20.8)	3.4 (0.6–17.2)
Ischaemic heart disease (%)	32.7 (24.3–42.3)	24.1 (12.2–42.1)
Peripheral arterial disease (%)	12.8 (7.5–21.0)	13.8 (5.6–30.6)
Intima-media thickness (mm)	0.85 (0.19)	0.97 (0.20)*

Data are presented as percentages (95% CI) or mean (SD). SDM, screening-detected diabetes mellitus; GPDM, diabetes mellitus newly diagnosed in general practice. *Significantly different from SDM ($P < 0.05$).

both groups, but GPDM men were significantly less likely to be overweight than SDM men. Microalbuminuria was more prevalent in GPDM men and women, although the difference was not statistically significant. GPDM men and women were more likely to smoke than SDM patients of either sex.

Table 2 shows the prevalence of macrovascular complications at the time of diagnosis in diabetic patients identified by screening and in general practice. Prior myocardial infarction and ischaemic heart disease were more frequently found in SDM patients than in GPDM patients, and the difference in ischaemic heart disease was statistically significant in women. The prevalence of peripheral arterial disease was slightly higher in SDM women than in GPDM women. No difference in the prevalence of peripheral arterial disease was observed between SDM and GPDM men. Mean intima-media thickness was significantly greater in GPDM men than in SDM men.

Discussion

Screening for type 2 diabetes is directed at the identification of patients at an early stage of the disease. Consequently, with screening one would expect to identify patients earlier in the development of hyperglycaemia than when they are newly diagnosed in general practice. Accordingly, diabetes-related complications are also expected to be less prevalent or less extensive in patients identified by screening. In this study, the only difference in macrovascular complications in the expected direction was the difference in intima-media thickness (lower in SDM than in GPDM patients), and significantly lower in men. The prevalence of peripheral arterial disease was similar in both groups of patients, whilst the prevalence of ischaemic heart disease and previous myocardial infarction was even higher in SDM patients. Although glucose and HbA1c levels were lower in SDM compared with GPDM patients, which might be an indication that SDM patients were identified earlier in the development of hyperglycaemia, other cardiovascular risk factors such as hypertension were more frequently present in SDM patients. This might be explained by the targeted screening approach. The screening questionnaire (SRQ) includes some cardiovascular items such as use of antihypertensive medication, shortness of breath and claudication. Consequently,

the SDM patients identified through targeted screening with the SRQ may be expected to have an unfavourable cardiovascular risk.

The difference in diagnostic procedure between SDM and GPDM patients might also contribute to the differences in the prevalence of macrovascular complications. In the SDM group, the diagnosis was based on elevated fasting and 2-h plasma glucose values whilst in the GPDM group it was based on elevated fasting plasma glucose values only. The diagnostic fasting glucose criteria for diabetes have been shown to be less predictive of cardiovascular disease [24] and mortality [3]. To investigate whether the difference in diagnostic procedure played a role in our findings, we compared the prevalence of myocardial infarction and ischaemic heart disease between GPDM patients and those SDM patients whose diagnosis was also based on fasting glucose values (thus excluding 36 SDM patients). The differences in the prevalence of myocardial infarction and ischaemic heart disease were similar to those observed for the entire SDM group (data not shown). Consequently, the difference in diagnostic procedure is unlikely to provide an explanation for our findings. Coverage of care has not influenced the study results because in the Netherlands everyone is insured for health care.

The low prevalence of previous myocardial infarction relative to the high intima-media thickness in the GPDM group is not in line with the reported positive association of intima-media thickness with coronary heart disease [25, 26]. A healthy survivor effect might have been present in the GPDM group, indicating that all those who had high intima-media thickness and myocardial infarction had already died, even before the start of the study. Other observations in our study, such as the difference between sexes in intima-media thickness and the positive associations with age and blood pressure (data not shown), were similar to those reported in the literature [26–29]. The low prevalence of myocardial infarction in the GPDM group might also indicate that diabetic patients who were newly diagnosed as a consequence of a recent myocardial infarction might not have been recruited for the study, although GPs were encouraged to recruit all newly diagnosed diabetic patients. The small sample size of the SDM and GPDM groups, the small number of patients with complications, and the resulting imprecision, might provide an additional explana-

ation for our findings. If the number of GPDM patients had been higher, the difference in intima-media thickness might have become statistically significant (men and women together). However, the similarity in prevalence of peripheral arterial disease and the difference in prevalence of myocardial infarction between the two groups might not have been easily affected by a higher number of GPDM patients.

Targeted screening implies the selection of a high-risk population for diagnostic testing. Compared with universal screening for type 2 diabetes, targeted screening might miss individuals who do have diabetes but do not have the risk factors included in the first noninvasive screening test, i.e. the young, less obese diabetic patients without a family history of diabetes and/or without cardiovascular symptoms. One might speculate that these missed patients may also have a lower prevalence of macrovascular complications. Most noninvasive screening tests for type 2 diabetes that can be used in targeted screening to select a high-risk population include obesity and at least one cardiovascular item (most frequently hypertension) [30–33]. Thus, the high-risk population identified by targeted screening is at risk of both diabetes and cardiovascular disease. This is illustrated by our previous finding that a positive result on the Cambridge Risk Score [31], a noninvasive screening test for type 2 diabetes, was associated with an increased mortality risk [34], independent of the presence of diabetes. Because of the identification of a population at high risk of both diabetes and of cardiovascular disease, targeted screening for type 2 diabetes might be an efficient alternative to a screening procedure that is restricted to hyperglycaemia alone. Future studies need to determine the cost-effectiveness of targeted screening strategies for type 2 diabetes.

In conclusion, targeted screening for type 2 diabetes identified diabetic patients with a prevalence of macrovascular complications similar to that found amongst newly diagnosed diabetic patients in general practice, but with a lower degree of hyperglycaemia. Our study is the first confirmation of the idea that targeted screening might be an efficient way to identify people at high risk of undiagnosed type 2 diabetes and of cardiovascular disease. However, results from studies that address the (cost)-effectiveness of early treatment following

detection by targeted screening need to be awaited before targeted screening can be recommended.

Conflict of interest statement

No conflict of interest was declared.

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