Use of the Diabetes Risk Score for Opportunistic Screening of Undiagnosed Diabetes and Impaired Glucose Tolerance

The IGLOO (Impaired Glucose Tolerance and Long-Term Outcomes Observational) study

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OBJECTIVE — To evaluate an opportunistic screening strategy addressed to individuals with one or more cardiovascular risk factor, based on the Diabetes Risk Score (DRS) as the initial instrument, for the identification of individuals with type 2 diabetes or impaired glucose tolerance (IGT).

RESEARCH DESIGN AND METHODS — The DRS, a simple self-administered questionnaire, was completed by individuals identified by general practitioners and presenting with one or more cardiovascular risk factor. All patients underwent a 2-h oral glucose tolerance test (OGTT). The optimal DRS cutoff was calculated by applying the receiver-operating characteristic curve.

RESULTS — Overall, 1,377 individuals aged between 55 and 75 years received an OGTT and completed the DRS. Mean DRS values showed a marked variation according to glucose metabolism categories, as follows: 8.7 ± 3.0 in normoglycemic individuals, 9.5 ± 3.1 in individuals with impaired fasting glucose, 9.9 ± 3.3 in individuals with IGT, and 12.0 ± 3.5 in individuals with type 2 diabetes. The receiver-operating characteristic curve showed that, with a cutoff of 9, the sensitivity of DRS in detecting individuals with glucose abnormalities (type 2 diabetes or IGT) was 77% and the specificity 45%. The use of the DRS as an initial screening instrument, followed by the measurement of fasting blood glucose in individuals with a score ≥9 and by the OGTT in individuals with a fasting blood glucose between 5.6 and 6.9 mmol/l, would lead to the identification of 83% of the case subjects with type 2 diabetes and 57% of the case subjects with IGT, at a cost of an OGTT in 38% of the sample and a fasting blood glucose in 64%.

CONCLUSIONS — The DRS can represent a valid inexpensive instrument for opportunistic screening and a useful alternative to indiscriminate fasting blood glucose measurement, not readily available in general practice.

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The prevalence of type 2 diabetes is rapidly growing worldwide (1,2). This condition exerts a pernicious effect on patient health and health care budgets, and early detection of subjects with undiagnosed diabetes might be important in reducing the burden of diabetic complications. This is of particular importance considering that diabetes is frequently not diagnosed until complications appear, and approximately one-third of all people with diabetes may be undiagnosed (3).

Recent experimental evidence has shown that type 2 diabetes can be prevented or delayed by implementing lifestyle modifications (e.g., diet and exercise) or using pharmacological treatment (metformin or acarbose) in individuals with impaired glucose tolerance (IGT) (4–7). These findings have provided the rationale for screening IGT. This condition is defined using a 2-h oral glucose tolerance test (OGTT), a kind of test that is often considered to entail enough discomfort to discourage its indiscriminate use. Identifying people at increased risk for undiagnosed diabetes or glucose intolerance, followed by blood glucose testing to establish diagnosis, is considered to be an appropriate way of dealing with this problem (8).

In the context of the IGLOO (Impaired Glucose Tolerance and Long-Term Outcomes Observational) study, we evaluated whether the Diabetes Risk Score (DRS) (9) could represent a valid inexpensive initial screening tool for the identification of individuals with unknown

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Additional information for this article can be found in an online appendix at http://care.diabetesjournals.org.

Abbreviations: AUC, area under the receiver-operating characteristic curve; CV, cardiovascular; DRS, Diabetes Risk Score; FBG, fasting blood glucose; IFG, impaired fasting glucose; IGLOO study, Impaired Glucose Tolerance and Long-Term Outcomes Observational study; IGT, impaired glucose tolerance; OGTT, oral glucose tolerance test.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

diabetes or glucose intolerance. The DRS was tested in the context of an opportunistic screening strategy, applied by general practitioners to individuals with one or more cardiovascular (CV) risk factor attending their offices.

We also tested the effectiveness of a three-step screening strategy to identify individuals with undiagnosed diabetes or IGT, while reducing the number of those needing an OGTT. This strategy was based on the DRS as the initial screening instrument, followed by the measurement of fasting blood glucose (FBG) and the execution of OGTT in selected subgroups.

RESEARCH DESIGN AND METHODS

The IGLOO study is a multicenter prospective cohort study aimed at estimating the prevalence of IGT and unknown diabetes in individuals with one or more CV risk factor and assessing the 5-year incidence of type 2 diabetes and CV events, according to their baseline CV and metabolic risk profile. The presented data refer to the cross-sectional validation of a screening strategy based on the DRS.

The study population was represented by men and women aged between 55 and 75 years, without a history of CV events (angina, myocardial infarction, percutaneous transluminal balloon coronary angioplasty/coronary artery bypass graft, heart failure, transient ischemic attack, stroke, peripheral vascular disease or limb bypass surgery, or percutaneous angioplasty) and with one or more of the following CV risk factors: family history of premature CV events (definite myocardial infarction or sudden death before 55 years of age in father or other male first-degree relative or before 65 years of age in mother or other female first-degree relative), hypertension (>140 mmHg systolic or >90 mmHg diastolic or on antihypertensive medication), dyslipidemia (total cholesterol ≥220 mg/dl or LDL cholesterol ≥160 mg/dl or HDL cholesterol <40 mg/dl or on lipid-lowering therapy), left ventricular hypertrophy with strain pattern defined per electrocardiogram (Sokolow and Lyon criteria or Cornell criteria), or smoking (current cigarette smoking or an individual who has quit smoking <12 months before inclusion). Presence of the metabolic syndrome was defined according to Adult Treatment Panel III criteria (10).

Consecutive patients up to a maximum of 30 individuals who attended the general practitioners' offices for a routine visit and met the eligibility criteria were identified. All patients were referred to a diabetes outpatient clinic to perform an OGTT, with determination of venous plasma glucose, fasting and 2 h after the ingestion of 75 g glucose. Immediately after being drawn, all samples were centrifuged, and aliquots were prepared within 1 h of collection. Plasma aliquots were stored at −20°C and then transferred on dry ice to the core laboratory (Servizio di Patologia Clinica, Ospedale di Desio, Milano) for central core laboratory analysis. Aliquots were frozen at −80°C until conduction of the analyses. Plasma glucose was analyzed using the enzymatic colorimetric method GOD-PAP on a Modular Analyzer (Roche Diagnostics). Coefficients of variation were 2.3 and 1.9% for fasting and postload glucose tests, respectively. At study entry, general practitioners collected clinical information for all enrolled patients and asked them to complete the DRS questionnaire before being referred to the diabetes clinic for the OGTT. All patients gave written informed consent before their participation in the study. Local ethical committees approved the protocol.

DRS

The original version of the questionnaire was developed to characterize individuals according to their future risk of developing type 2 diabetes (9). Furthermore, the authors have evaluated the usefulness of the DRS in detecting asymptomatic diabetes in a cross-sectional setting.

The DRS is a simple fast self-administered questionnaire (a copy of the DRS is provided at http://care.diabetesjournals.org). It is based on the presence of well-known diabetes risk factors; in particular, the questionnaire collected information about age, BMI, waist circumference, use of blood pressure medication, history of high blood glucose, physical activity, and daily consumption of vegetables, fruits, or berries. The DRS system does not need clinical data collected by physicians. The score ranges between 0 and 20, and a cut point of 9 best identifies individuals at higher risk of developing type 2 diabetes, with a sensitivity of 0.78–0.81 and a specificity of 0.76–0.77. For the detection of prevalent diabetes, the sensitivity of DRS was 0.76–0.77, the specificity was 0.66–0.67, the positive predictive value was 0.07–0.12, and the negative predictive value was 0.98–0.99 (9).

Statistical analysis

The statistical analysis was performed using the SPSS statistical software release 10.1 (SPSS, Chicago, IL).

Patients' characteristics according to DRS classes were compared using the Kruskal-Wallis one-way ANOVA for continuous variables and the χ^2 test for categorical variables. Sensitivity (percentage of individuals with undiagnosed type 2 diabetes or glucose abnormalities who had a positive screening test), specificity (percentage of individuals without undiagnosed type 2 diabetes or glucose abnormalities who had a negative screening test), and predictive values were calculated for the different tests. The positive predictive value was calculated as the proportion of individuals with a positive test who had type 2 diabetes or glucose abnormalities, whereas the negative predictive value represents the proportion of individuals with a negative test without type 2 diabetes or glucose abnormalities. Because predictive values strongly depend on the prevalence of the target disorder, we also calculated positive and negative likelihood ratios. The positive likelihood ratio is the ratio of true-positive rate to false-positive rate and indicates how much more likely a positive test is to be found in an individual with, as opposed to an individual without, the condition. The negative likelihood ratio is the ratio of false-negative to true-negative rate and indicates how likely a negative test is to be found in an individual with, as opposed to an individual without, the condition. The higher the positive likelihood ratio, and the lower the negative likelihood ratio, the more the test is able to discriminate people with and without the condition of interest. The 95% CIs for sensitivity, specificity, predictive values, and likelihood ratios were also estimated (11).

To determine the optimal DRS cutoff for the detection of type 2 diabetes and glucose abnormalities, we calculated the receiver-operating characteristic curves by plotting the sensitivity of the test versus the false-positive rate (1 − specificity). The cutoff is chosen to maximize the true-positive rate while minimizing the false-positive rate (12). The area under the receiver-operating characteristic

curve (AUC) with its 95% CIs was also estimated. The AUC quantifies how well the test correctly distinguishes a subject with diabetes or glucose abnormalities from a subject without the condition; the larger the area under the curve, the better the performance of the test.

All the tests were performed using the World Health Organization 1999 criteria (13) for the definition of type 2 diabetes and IGT as the gold standard.

To evaluate the likely behavior of the proposed screening strategies in populations with a lower prevalence of glucose abnormalities (IGT + type 2 diabetes), we modeled their effectiveness in terms of number of cases detected and costs when applied in populations with a prevalence of 20, 10, and 5%. These analyses were performed under the plausible assumption that the sensitivity and the specificity of any screening strategy are not affected by the prevalence of the target condition in the population being screened (12).

We only estimated the direct costs of laboratory tests, with reference to the published Italian health care system fees (€7.59 for OGTT and €3.87 for FBG).

RESULTS — Overall, 1,840 individuals were recruited by 109 general practitioners; of the patients enrolled, 210 did not undergo the OGTT, 217 did not fill in the DRS questionnaire, and 36 lacked both pieces of information, leaving a total of 1,377 patients who could be evaluated (74.5%).

Patients excluded from the analyses did not differ from those included in terms of age, BMI, waist circumference, systolic and diastolic blood pressure, levels of cholesterol and triglycerides, presence of hypertension, dyslipidemia, family history of premature coronary heart disease, smoking habits, and presence of metabolic syndrome. Patients not included were less often men (45.6 vs. 51.7%; $P = 0.02$) and were more likely to present with left ventricular hypertrophy (13.1 vs. 8.9%, $P = 0.009$) than those included.

Patient characteristics are reported in Table 1. Overall, 54.9% of the patients showed some forms of glucose metabolism alteration; in particular, 15.4% of the patients had impaired fasting glucose (IFG), 11.1% had IGT, 11.0% had IGT and IFG, and 17.4% had diabetes. According to the recent American Diabetes Association criteria, a more stringent FBG value (<5.6 mmol/l) is indicated to define normoglycemia (14). If the new American Diabetes Association criteria were applied, the proportion of patients with IGT classified as normal would decrease to 21.6%; on the other hand, 55.7% of the subjects classified as normal with the World Health Organization criteria would have IFG, and the overall proportion of individuals classified as normal would fall to 32.1%.

We found a strong correlation between DRS classes, as defined in the original article by Lindström and Tuomilehto (9), and CV risk factor distribution (Table 1). In particular, the prevalence of all the components of the metabolic syndrome tended to dramatically increase with increasing DRS values. On the other hand, individuals with lower DRS values showed higher total cholesterol levels and were more often smokers than individuals with higher DRS values.

Mean DRS values showed a marked variation according to glucose metabolism categories, as follows: 8.7 ± 3.0 in normoglycemic individuals, 9.5 ± 3.1 in individuals with IFG, 9.9 ± 3.3 in individuals with IGT, 10.3 ± 3.3 in individuals with IFG and IGT, and 12.0 ± 3.5 in individuals with type 2 diabetes ($P < 0.0001$).

The receiver-operating characteristic curve showed that a cutoff of 9 ensured the best balance between true-positive and false-positive rates. In fact, with a cutoff of 9, the sensitivity of DRS in detecting individuals with glucose abnormalities was 77%, whereas the specificity was 45% (AUC = 0.67; 95% CI 0.64–0.70). The sensitivity and specificity for the detection of type 2 diabetes alone, with the cut point of 9, were 86 and 41%, respectively (AUC = 0.72; 95% CI 0.68–0.76). Therefore, despite the high prevalence of glucose metabolism alterations in our study sample, a cutoff of 9 had a negative predictive value of 76% for glucose abnormalities and 93% for type 2 diabetes (Table 2).

As for FBG, in our sample, an FBG ≥6.1 mmol/l had a sensitivity of 92% and a specificity of 68% for the diagnosis of type 2 diabetes, whereas for the diagnosis of glucose abnormalities, the sensitivity was 68% and the specificity 75%. With an FBG cutoff of 5.6 mmol/l, the sensitivity for the diagnosis of type 2 diabetes was 97% and the specificity was 38%, whereas for the diagnosis of glucose abnormalities, the sensitivity was 86% and the specificity was 44%.

The combined use of FBG and DRS values led to an improvement in the detection rate of unknown diabetes and glucose abnormalities (Table 2). In particular, using the DRS in combination with an FBG cutoff of ≥6.1 mmol/l led to an increase in sensitivity, which reached 99% for the diagnosis of type 2 diabetes and 90% for the diagnosis of glucose abnormalities (both tests negative), whereas the specificity was 78% for the diagnosis of type 2 diabetes and 84% for the diagnosis of glucose abnormalities (both tests positive). The negative predictive value, when both tests were negative, was 99% for the diagnosis of type 2 diabetes and 85% for the diagnosis of glucose abnormalities. When we adopted the FBG cutoff level of ≥5.6 mmol/l, the sensitivity was further improved (100% for the diagnosis of type 2 diabetes and 95% for glucose abnormalities), but the specificity decreased to 59% for the detection of type 2 diabetes and 65% for glucose abnormalities. The negative predictive value, when both tests were negative, was 100% for the diagnosis of type 2 diabetes and 88% for the diagnosis of glucose abnormalities.

The likelihood of finding both tests positive was more than three times higher in the presence of a glucose abnormality, when using an FBG cutoff of 6.1 mmol/l, whereas the likelihood of finding both tests negative was five times higher for individuals without glucose abnormalities when using an FBG cutoff of 5.6 mmol/l.

Based on our results, we hypothesized different screening strategies to be applied to high-risk individuals. The first is based on FBG testing in all patients, the second on the administration of the DRS as an initial screening tool, with FBG measured only in individuals with a score ≥9. As a third step, we further differentiated the need for OGTT according to two different levels of FBG (i.e., OGTT performed in individuals with FBG between 6.1 and 6.9 mmol/l or FBG between 5.6 and 6.9 mmol/l). A strategy based on the DRS as an initial screening instrument, with FBG measured only in individuals with a score ≥9, and an OGTT performed in individuals with an FBG value ≥5.6 mmol/l would lead to the identification of 83% of cases of unknown diabetes and 57% of cases of IGT. This strategy would require the measurement of FBG in 64%

Table 1—*Patient characteristics according to DRS classes*

	Overall sample	DRS				
		Score 0–3	Score 4–8	Score 9–12	Score 13–20	*P*
n	1,377	49	447	655	226	
Men	712 (51.7)	26 (53.1)	240 (53.7)	336 (51.3)	110 (48.7)	0.7
Age (years)	62.4 ± 5.3	62.6 ± 5.3	62.0 ± 5.3	62.6 ± 5.3	62.9 ± 5.3	0.1
BMI						
Men	28.2 ± 6.4	23.4 ± 1.2	25.6 ± 2.2	29.4 ± 8.3	30.8 ± 3.8	<0.0001
Women	27.3 ± 4.6	21.1 ± 2.4	24.4 ± 2.7	28.1 ± 3.9	31.6 ± 4.7	<0.0001
Waist circumference (cm)						
Men	100.6 ± 11.7	87.3 ± 5.9	93.3 ± 9.9	104.0 ± 9.5	109.3 ± 10.7	<0.0001
Women	91.8 ± 12.1	73.0 ± 5.2	83.1 ± 8.5	95.1 ± 9.4	102.1 ± 11.1	<0.0001
Triglycerides (mmol/l)	1.54 ± 0.87	1.23 ± 0.51	1.44 ± 0.78	1.58 ± 0.92	1.69 ± 0.91	<0.0001
Total cholesterol (mmol/l)	5.8 ± 0.98	5.80 ± 0.94	5.92 ± 0.93	5.84 ± 1.02	5.68 ± 0.97	0.03
HDL cholesterol (mmol/l)	1.42 ± 0.36	1.52 ± 0.40	1.48 ± 0.37	1.40 ± 0.36	1.33 ± 0.32	<0.0001
LDL cholesterol (mmol/l)	3.72 ± 0.87	3.72 ± 0.86	3.77 ± 0.84	3.73 ± 0.90	3.60 ± 0.84	0.1
Systolic blood pressure (mmHg)	138.3 ± 15.1	126.4 ± 19.2	133.9 ± 13.2	141.2 ± 15.0	141.0 ± 15.1	<0.0001
Diastolic blood pressure (mmHg)	84.0 ± 7.8	80.3 ± 6.2	82.0 ± 7.5	85.1 ± 7.6	85.6 ± 8.0	<0.0001
Blood glucose (mmol/l)						
Fasting	6.07 ± 1.19	5.66 ± 0.53	5.77 ± 0.92	6.09 ± 1.05	6.71 ± 1.78	<0.0001
2 h postload	7.70 ± 3.04	6.63 ± 1.80	6.74 ± 2.16	7.81 ± 2.90	9.53 ± 4.11	<0.0001
Waist circumference						
Men ≥102 cm; women ≥88 cm	680 (49.4)	0	74 (16.6)	419 (64.0)	187 (82.7)	<0.0001
Cardiovascular risk factors						
Hypertension	835 (60.8)	8 (16.3)	173 (38.8)	468 (71.8)	186 (82.3)	<0.0001
Dyslipidemia	925 (67.5)	41 (83.7)	325 (73.0)	409 (62.7)	150 (66.7)	0.0003
Smoking	288 (20.9)	9 (18.4)	120 (26.9)	121 (18.5)	38 (16.8)	0.003
Family history (CV events)	171 (12.4)	8 (16.3)	52 (11.6)	90 (13.7)	21 (9.3)	0.3
Left ventricular hypertrophy	123 (8.9)	1 (2.0)	21 (4.7)	67 (10.2)	34 (15.0)	<0.0001
Glucose metabolism						
NGT	621 (45.1)	29 (59.2)	268 (60.0)	269 (41.1)	55 (24.3)	
IFG	212 (15.4)	7 (14.3)	68 (15.2)	112 (17.1)	25 (11.1)	
IGT	153 (11.1)	8 (16.3)	42 (9.4)	78 (11.9)	25 (11.1)	<0.0001
IGT + IFG	152 (11.0)	3 (6.1)	38 (8.5)	79 (12.1)	32 (14.2)	
Type 2 diabetes	239 (17.4)	2 (0.8)	31 (7.0)	117 (17.9)	89 (39.4)	
Number of components of metabolic syndrome*						
0	123 (8.9)	19 (38.8)	83 (18.6)	17 (2.6)	4 (1.8)	
1	322 (23.4)	19 (38.8)	159 (35.6)	127 (19.4)	17 (7.5)	
2	430 (31.2)	10 (20.4)	136 (30.4)	227 (34.7)	57 (25.2)	<0.0001
3	309 (22.4)	1 (2)	49 (11.0)	173 (26.4)	86 (38.1)	
4	130 (9.4)	—	20 (4.5)	73 (11.1)	37 (16.4)	
5	63 (4.6)	—	—	38 (5.8)	25 (11.1)	
Number of CV risk factors						
1	596 (44.0)	29 (61.7)	234 (53.8)	264 (40.7)	69 (30.9)	
2	561 (41.4)	16 (34.0)	157 (36.1)	279 (43.0)	109 (48.9)	<0.0001
3	168 (12.4)	2 (4.3)	36 (8.3)	91 (14.0)	39 (17.5)	
≥4	29 (2.1)	—	8 (1.8)	15 (2.3)	6 (2.7)	

Data are means ± SE or *n* (%). *According to the Adult Treatment Panel III criteria. NGT, normal glucose tolerance.

of the patients and an OGTT in 38%. On the other hand, a strategy based on FBG measurement in all individuals and the performance of OGTT in those with an FBG ≥5.6 mmol/l would allow the identification of 97% of type 2 diabetic subjects and 78% of individuals with IGT, but 56% of the patients should undergo an oral test. The yield of the different screening strategies is summarized in Table 3, where we report the results obtained in the IGLOO population as well as those deriving from the simulations based on different scenarios, with a prevalence of glucose abnormalities ranging between 5 and 20%. From the table it emerges that the best compromise between number of cases detected and cost per case detected is represented by the screening strategy using the DRS as initial instrument, with an FBG performed in individuals with a

DRS score ≥9 and an OGTT performed in individuals with an FBG between 5.6 and 7 mmol/l. Furthermore, the difference in cost per case detected in favor of DRS as the initial screening tool tended to increase as the prevalence of the target condition decreased.

CONCLUSIONS — Recent evidence from several randomized trials, showing that diabetes can be prevented or delayed by lifestyle modification or pharmacological interventions in individuals with IGT, has provided the rationale for screening IGT. To avoid unnecessary costs and the inconvenience related to glucose oral tests, it is of primary importance to identify high-risk patients more likely to benefit from the OGTT results.

While several strategies have been developed for the identification of individuals at higher risk of having or developing diabetes (15–20), only a few studies have addressed the problem of also identifying those with asymptomatic hyperglycemia requiring clinical intervention (21,22). In particular, in the Atherosclerosis Risk in Communities (ARIC) study, a clinical detection rule was developed that, associated with FPG and/or OGTT, led to the detection of 86.3% of the cases of diabetes and 52.4% of the cases of IGT, with 39.6% of the patients needing an OGTT (assuming that patients with IFG needed to be reclassified) (21). The major limitations of this approach are related to the inclusion of African-American ethnicity, which limits its use in non-U.S. settings, and the complexity of the clinical detection rules, which make its use particularly difficult in general practice.

Our data show that the DRS, initially validated in a Finnish population, can represent a simple and valid tool, even in a Mediterranean population. Interestingly, the same cutoff identified in the Finnish population for the prediction of type 2 diabetes development was also able to discriminate cross-sectionally those individuals who were more likely to present glucose abnormalities.

To be used as an initial screening tool, an instrument should have sufficient sensitivity to avoid too many patients being classified as normal despite the presence of the disease. In our study, the questionnaire was tested in patients with one or more CV risk factor; despite the very high pretest probability of disease, a cutoff of 9 had a sensitivity of 86% and a negative

Table 2—*Performance of DRS and FBG, alone or in combination, for the identification of diabetes and glucose abnormalities (diabetes or IGT)*

	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Positive likelihood ratio	Negative likelihood ratio
Diabetes						
DRS >9	0.86 (0.82–0.91)	0.41 (0.38–0.44)	0.23 (0.21–0.26)	0.93 (0.91–0.96)	1.45 (1.35–1.56)	0.34 (0.25–0.47)
FBG ≥5.6 mmol/l	0.97 (0.95–0.99)	0.38 (0.35–0.41)	0.25 (0.22–0.28)	0.98 (0.97–1.0)	1.57 (1.49–1.65)	0.08 (0.04–0.16)
FBG ≥6.1 mmol/l	0.92 (0.88–0.95)	0.68 (0.65–0.71)	0.38 (0.34–0.41)	0.97 (0.96–0.99)	2.86 (2.61–3.14)	0.12 (0.08–0.12)
DRS + FBG ≥6.1 mmol/l						
Both positive	0.79 (0.74–0.84)	0.78 (0.76–0.81)	0.43 (0.39–0.48)	0.95 (0.93–0.96)	3.63 (3.19–4.12)	0.27 (0.21–0.34)
Both negative	0.99 (0.97–1.00)	0.30 (0.28–0.33)	0.23 (0.20–0.26)	0.99 (0.98–1.00)	1.42 (1.36–1.48)	0.04 (0.01–0.13)
DRS + FBG ≥5.6 mmol/l						
Both positive	0.83 (0.79–0.88)	0.59 (0.56–0.62)	0.30 (0.27–0.34)	0.94 (0.93–0.96)	2.04 (1.87–2.23)	0.28 (0.21–0.38)
Both negative	1.00	0.20 (0.17–0.22)	0.21 (0.18–0.23)	1.00	1.25 (1.21–1.28)	0
Diabetes or IGT						
DRS >9	0.77 (0.74–0.81)	0.45 (0.41–0.48)	0.48 (0.44–0.51)	0.76 (0.71–0.79)	1.40 (1.29–1.51)	0.51 (0.43–0.61)
FBG ≥5.6 mmol/l	0.86 (0.84–0.89)	0.44 (0.41–0.48)	0.50 (0.47–0.54)	0.83 (0.8–0.87)	1.55 (1.45–1.67)	0.3 (0.24–0.38)
FBG ≥6.1 mmol/l	0.68 (0.64–0.72)	0.75 (0.72–0.78)	0.64 (0.60–0.68)	0.78 (0.75–0.81)	2.68 (2.35–3.05)	0.43 (0.37–0.49)
DRS + FBG ≥6.1 mmol/l						
Both positive	0.55 (0.51–0.59)	0.84 (0.81–0.86)	0.69 (0.64–0.73)	0.74 (0.71–0.77)	3.35 (2.83–3.98)	0.54 (0.49–0.59)
Both negative	0.90 (0.88–0.93)	0.78 (0.76–0.81)	0.48 (0.45–0.51)	0.85 (0.81–0.89)	1.40 (1.32–1.49)	0.27 (0.21–0.36)
DRS + FBG ≥5.6 mmol/l						
Both positive	0.69 (0.65–0.73)	0.65 (0.62–0.69)	0.56 (0.53–0.60)	0.76 (0.73–0.79)	1.98 (1.78–2.21)	0.48 (0.42–0.55)
Both negative	0.95 (0.93–0.97)	0.24 (0.21–0.27)	0.55 (0.42–0.48)	0.88 (0.84–0.92)	1.24 (1.19–1.30)	0.21 (0.14–0.31)

Data are value (95% CI).

Table 3—*Yield of different screening strategies for the detection of type 2 diabetes and IGT*

	Cases of IGT + type 2 diabetes detected [*n* (%)]	FBG measurements performed (*n*)	OGTTs performed (*n*)	FBG measurements per case detected (*n*)	OGTTs per case detected (*n*)	Total cost (Euros)	Cost per case detected (Euros)
IGLOO population: prevalence of IGT + type 2 diabetes = 39.5%							
FBG, if 5.6 < FBG < 7 mmol/l, then OGTT	344 (87)	1,000	558	2.9	1.6	8,105.2	23.56
FBG, if 6.1 < FBG < 7 mmol/l, then OGTT	269 (68)	1,000	300	3.7	1.1	6,147	22.85
DRS; if DRS ≥9, then FBG; if 5.6 < FBG < 7 mmol/l, then OGTT	273 (69)	640	380	2.4	1.4	5,361	19.6
DRS; if DRS ≥9, then FBG; if 6.1 < FBG < 7 mmol/l, then OGTT	217 (55)	640	210	2.9	1.1	4,070.7	18.75
Prevalence of IGT + type 2 diabetes = 20%							
FBG, if 5.6 < FBG < 7 mmol/l, then OGTT	174 (87)	1,000	558	5.7	3.2	8,105.2	46.58
FBG, if 6.1 < FBG < 7 mmol/l, then OGTT	136 (68)	1,000	280	7.4	2.0	5,995.2	44.08
DRS; if DRS ≥9, then FBG; if 5.6 < FBG < 7 mmol/l, then OGTT	138 (69)	590	360	4.3	2.6	5,015.7	36.35
DRS; if DRS ≥9, then FBG; if 6.1 < FBG < 7 mmol/l, then OGTT	110 (55)	590	190	5.4	1.7	3,725.4	33.86
Prevalence of IGT + type 2 diabetes = 10%							
FBG, if 5.6 < FBG < 7 mmol/l, then OGTT	87 (87)	1,000	556	11.5	6.4	8,090	92.99
FBG, if 6.1<FBG<7 mmol/l, then OGTT	68 (68)	1,000	270	14.7	3.9	5,919.3	87.05
DRS; if DRS ≥9, then FBG; if 5.6 < FBG < 7 mmol/l, then OGTT	69 (69)	570	350	8.3	5.1	4,862.4	70.47
DRS; if DRS ≥9, then FBG; if 6.1 < FBG < 7 mmol/l, then OGTT	55 (55)	570	180	10.4	3.2	3,572.1	64.95
Prevalence of IGT + type 2 diabetes = 5%							
FBG, if 5.6 < FBG < 7 mmol/l, then OGTT	44 (87)	1,000	557	23.0	12.8	8,097.6	184.04
FBG, if 6.1 < FBG < 7 mmol/l, then OGTT	34 (68)	1,000	260	29.4	7.7	5,843.4	171.86
DRS; if DRS ≥9, then FBG; if 5.6 < FBG < 7 mmol/l, then OGTT	35 (69)	560	350	16.3	10.1	4,823.7	137.82
DRS; if DRS ≥9, then FBG; if 6.1 < FBG < 7 mmol/l, then OGTT	28 (55)	560	170	20.4	6.2	3,457.5	123.48

Estimates refer to 1,000 individuals screened.

predictive value of 93% for undiagnosed diabetes, whereas for glucose abnormalities, the sensitivity and the negative predictive values were 77 and 76%, respectively. Therefore, it is reasonable to assume that the negative predictive value of the test be even greater when applied to a population with lower pretest probability of the disease. When applied in combination with an FPG cutoff of 6.1 mmol/l, the test also showed acceptable specificity (78% for the detection of type 2 diabetes and 84% for glucose abnormalities).

The use of the DRS as an initial screening instrument, followed by the measurement of FBG in individuals with a score ≥9 and by the OGTT in individuals with an FBG between 5.6 and 6.9 mmol/l, would lead to the identification of 83% of the cases of unknown diabetes and 57% of IGT cases, at a cost of an OGTT in 38% of the sample and an FBG in 64%. Therefore, the yield of this strategy would be almost identical to that obtained in the ARIC study (21), but with a much simpler and less expensive approach, considering that only two-thirds of the patients needed the FBG measurement with our strategy. It is important to note that the same detection rate would be obtained with a strategy using an FBG measurement as the initial step, followed by an OGTT in individuals with an FBG of 6.1–6.9 mmol/l. Nevertheless, the cost per case detected of this strategy would be higher than that based on the DRS as the initial screening instrument. The highest detection rate would be obtained using the FBG measurement as a first step and applying an OGTT to individuals with an FBG between 5.6 and 6.9 mmol/l. This strategy would allow the identification of 97% of the cases of type 2 diabetes and 78% of the cases of IGT, but 56% of the individuals would require an OGTT, and the cost per case detected would therefore increase proportionally. The best strategy to apply in a specific setting will thus depend on the resources available, as well as on the possibility to test FBG in all the patients. When FBG cannot be easily measured, the DRS can represent a valid and inexpensive alternative. It can be particularly useful as an instrument for opportunistic screening in general practice, since the measurement of FBG is not readily available in many general practitioners' offices. In these circumstances, considering that referring a patient to an external laboratory is costly and time-consuming, filling in the DRS may encourage an individual who gets a high value to have his or her blood glucose measured.

Finally, study limitations need to be discussed. First of all, patients were identified among those attending general practitioners offices and thus represent a situation similar to opportunistic screening, rather than population screening. Furthermore, they were selected on the basis of their CV risk profile, and only individuals in a restricted age range (i.e., 55–75 years) were included. Therefore, the generalizability of our findings could be limited.

As a second point, as in almost all published studies, we defined cases of diabetes and IGT on the basis of a single measurement, rather than using the repeated measurement required for a clinical diagnosis. Therefore, the yield of the different strategies in terms of cases detected could be overestimated.

In conclusion, our study shows that a very simple and inexpensive questionnaire, completed without any specific measurements and applied to individuals with one or more CV risk factor, performs well in identifying individuals at higher risk of unknown diabetes or IGT. When used in combination with FBG, the questionnaire allowed the identification of the vast majority of individuals with type 2 diabetes and >50% of those with IGT, while limiting the rate of those requiring an OGTT. It can thus represent a valuable tool for opportunistic screening in general practice. Whether the questionnaire performs equally well in populations at lower risk of diabetes and IGT remains to be proven.

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APPENDIX

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