# An Accurate Risk Score Based on Anthropometric, Dietary, and Lifestyle Factors to Predict the Development of Type 2 Diabetes

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**OBJECTIVE** — We aimed to develop a precise risk score for the screening of large populations for individuals at high risk of developing type 2 diabetes based on noninvasive measurements of major risk factors in German study populations.

**RESEARCH DESIGN AND METHODS** — A prospective cohort study (European Prospective Investigation into Cancer and Nutrition [EPIC]-Potsdam study) of 9,729 men and 15,438 women aged 35–65 years was used to derive a risk score predicting incident type 2 diabetes. Multivariate Cox regression model coefficients were used to weigh each variable in the calculation of the score. Data from the EPIC-Heidelberg, the Tübingen Family Study for Type 2 Diabetes (TÜF), and the Metabolic Syndrome Berlin Potsdam (MeSyBePo) study were used to validate this score.

**RESULTS** — Information on age, waist circumference, height, history of hypertension, physical activity, smoking, and consumption of red meat, whole-grain bread, coffee, and alcohol formed the German Diabetes Risk Score (mean 446 points [range 118–983]). The probability of developing diabetes within 5 years in the EPIC-Potsdam study increased from 0.3% for 300 to 23.2% for 750 score points. The area under the receiver-operator characteristic (ROC) curve was 0.84 in the EPIC-Potsdam and 0.82 in the EPIC-Heidelberg studies. Correlation coefficients between the German Diabetes Risk Score and insulin sensitivity in nondiabetic individuals were −0.56 in the TÜF and −0.45 in the MeSyBePo studies. ROC values for undiagnosed diabetes were 0.83 in the TÜF and 0.75 in the MeSyBePo studies.

**CONCLUSIONS** — The German Diabetes Risk Score (available at www.dife.de) is an accurate tool to identify individuals at high risk for or with undiagnosed type 2 diabetes.

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**Abbreviations:** AUC, area under the curve; ARIC, Atherosclerosis Risk in Communities; EPIC, European Prospective Investigation into Cancer and Nutrition; MeSyBePo, Metabolic Syndrome Berlin Potsdam; OGTT, oral glucose tolerance test; ROC, receiver-operator characteristic; TÜF, Tübingen Family Study for Type 2 Diabetes.

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

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Randomized clinical trials have demonstrated that type 2 diabetes can largely be prevented through diet and lifestyle modifications (1–4) or drug treatment (3,5). Personalized primary prevention among high-risk individuals to prevent the transition to overt diabetes is therefore a feasible and attractive alternative to reduce diabetes-related morbidity and mortality. The major challenge is how to identify those high-risk individuals, and, thus, several risk scores have been developed based on data from the San Antonio Heart Study (6), the Finrisk studies (7), the Japanese American Community Diabetes Study (8), the Atherosclerosis Risk in Communities (ARIC) study (9), the Rancho Bernardo Study (10), and a population-based survey in Umea, Sweden (11). Only the Finrisk studies (7) and the ARIC study (9) relied only on factors that are measurable with noninvasive methods and are therefore applicable outside of clinical practice. However, the ARIC risk score demonstrated relatively low validity in the testing sample (9). Furthermore, the Finrisk score recently has been tested in the German Cooperative Health Research in the Region of Augsburg Survey 2000, yielding a low validity to identify undiagnosed diabetic cases (12). Lack of inclusion of important risk factors (e.g., smoking and alcohol consumption) in the ARIC and Finrisk score and underestimation of the predictive information of important risk factors like age and waist circumference by the use of broad categories in Finrisk may explain its low validity. We therefore developed a risk score predicting the development of diabetes based on anthropometric, dietary, and lifestyle risk factors, including smoking and alcohol consumption, and evaluated the score in three additional German study populations. In contrast to the Finrisk score, we did not use broad categories for age and anthropometric risk factors in order to use the full information from these continuous variables.

## RESEARCH DESIGN AND METHODS

### European Prospective Investigation into Cancer and Nutrition-Potsdam study

The European Prospective Investigation into Cancer and Nutrition (EPIC)-Potsdam study (13) includes 27,548 participants, 16,644 women aged mainly 35–65 years and 10,904 men aged mainly 40–65 years, from the general population of Potsdam, Germany, recruited between 1994 and 1998 (14). The baseline examination included anthropometric measurements, a personal interview, and a questionnaire on prevalent diseases and sociodemographic and lifestyle characteristics, as well as a validated semiquantitative food frequency questionnaire (15). Frequency of food intake was measured using 10 categories, ranging from "never" to "five times per day or more." Portion sizes were estimated using photographs of standard portion sizes. Information on frequency of intake and portion size was used to calculate the amount of each food, in grams, consumed on average per day. Corrected correlation coefficients between the questionnaire and 12 24-h dietary recalls for bread, meat, coffee/tea, processed meat, fruits, vegetables, and alcohol consumption were 0.73, 0.65, 0.72, 0.70, 0.51, 0.48, and 0.94, respectively (16,17). Only 5% of underreporters of alcohol intake were observed, and correlation between reported intake from 24-h recalls and hydroxytryptophol: 5-hydroxyindol-3-acetic acid among the remaining 95% was 0.92 (18). Sport activities, biking, and gardening, reported separately for summer and winter, were calculated as the average time spent per week during the 12 months before baseline recruitment. The physical activity questionnaire has been developed for the EPIC and validated in a Dutch pilot study. Correlation coefficients for energy expenditure between the questionnaire and diaries were 0.28–0.55 for sport activities, 0.46–0.49 for biking, and 0.35–0.50 for gardening (19). The interview included a detailed assessment of present and past quantity and type of smoking. Additionally, age of onset and end of smoking as well as past smoking periods were assessed (20). Follow-up questionnaires have been administered every 2–3 years. Response rates for follow-up rounds exceed 90%. Incident cases of diabetes were identified through August 2005 via self-reports of a diabetes diagnosis, diabetes-relevant medication, or dietary treatment due to diabetes. All cases were verified by the diagnosing physician using ICD-10. After exclusion of participants with prevalent self-reported diabetes during follow-up but without physician's confirmation, with missing follow-up time and with missing covariate information at baseline, 9,729 men and 15,438 women remained for analyses. During an average of 7.0 years of follow-up we observed 849 incident cases of type 2 diabetes.

### The EPIC-Heidelberg study

The EPIC-Heidelberg study includes 25,540 participants with an age range similar to the EPIC-Potsdam study and similar recruitment procedures (13). Procedures to measure risk factors were identical to the EPIC-Potsdam. Cases of incident diabetes were identified by self-reported diagnosis and by reviewing medical records and death certificates. The validity of the case ascertainment was documented in a pilot study, where for 49 of 50 participants information from the treating physician could be obtained; 45 (91.8%) were confirmed as incident cases of type 2 diabetes and 2 were diagnosed around recruitment. A total of 23,398 participants remained after exclusion of those with prevalent diabetes, missing follow-up time, or missing covariate information and those reporting diabetic medication without a self-reported diagnosis during follow-up. Six hundred fifty-eight incident cases were identified during the first 5 years of follow-up.

### Tübingen Family Study for Type 2 Diabetes

Participants were recruited from the ongoing Tübingen Family Study for Type 2 Diabetes (TÜF) (21), which currently includes ~1,500 individuals. All participants underwent the standard procedures of the protocol including medical history, physical examination, assessment of smoking status, alcohol consumption habits and activity, routine blood test, and an oral glucose tolerance test (OGTT) after a 10-h overnight fast. Participants ingested a solution containing 75 g dextrose, and venous blood samples were obtained at 0, 30, 60, 90, and 120 min for determination of plasma glucose and plasma insulin. All subjects completed a standardized self-administered and validated questionnaire to measure physical activity (22). A complete set of data (except dietary information) was available from 657 healthy nondiabetic participants (222 men and 435 women, mean age 37 years) and 29 participants with undiagnosed diabetes.

### Metabolic Syndrome Berlin Potsdam study

The Metabolic Syndrome Berlin Potsdam (MeSyBePo) study includes 1,284 participants with unknown status of glucose metabolism aged >18 years. All participants underwent a physical examination, fasting blood was taken, and a 2-h OGTT was performed with a solution containing 75 g dextrose in the nondiabetic participants. Capillary glucose and serum insulin were determined in 30-min intervals during the OGTT. Anthropometry was performed by trained staff under standardized conditions. Medical history, smoking status, and alcohol consumption were asked by a questionnaire, and vigorous sporting activity was assessed according to Paffenbarger et al. (23). A complete set of data (except dietary information) was available from 863 nondiabetic participants (247 men and 616 women, mean age 51 years) and 148 participants with undiagnosed diabetes.

### Statistical analyses

We produced risk functions for detecting incident diabetes on the EPIC-Potsdam study cohort using Cox regression models with forward selection. Risk factors considered were age, sex, weight, height, BMI, waist circumference, self-reported history of hypertension, alcohol consumption (0, 0.1–5.0, 5.1–10.0, 10.1–40.0, or >40.0 g/day), physical activity (hours per week), occupational activity (light, moderate, or heavy), education (in or no training, vocational training, technical school, technical university, or university degree), smoking (never, past, current <20 cigarettes/day, or current ≥20 cigarettes/day), and the intake of processed meat, red meat, whole-grain bread, fruits, vegetables, and coffee. We also included terms for log-transformed age and waist circumference as well as interaction terms between sex and height and waist circumference in the model. To calculate absolute risks of developing diabetes within 5 years, we estimated the baseline hazard function [$h_0(t)$] from the Cox model for this time period in the EPIC-Potsdam study. Coefficients ($\beta$) of the model were used to assign a score value for each variable, and the German Diabetes Risk Score was calculated as the sum of those scores. The points from this score were used to estimate the probability ($P$)

**Table 1—*Risk factors of type 2 diabetes in the EPIC-Potsdam study with 25,167 participants (849 of whom developed diabetes)***

| Risk factor | β | Relative risk (95% CI) | *P* | Points allocated |
|---|---|---|---|---|
| Waist circumference (cm) | 0.074 | 1.076 (1.071–1.082) | <0.0001 | 7.4 |
| Height (cm) | −0.024 | 0.976 (0.967–0.984) | <0.0001 | −2.4 |
| Age (years) | 0.043 | 1.044 (1.035–1.053) | <0.0001 | 4.3 |
| Hypertension (self-report) | 0.462 | 1.587 (1.375–1.831) | <0.0001 | 46 |
| Intake of red meat (each 150 g/day) | 0.494 | 1.639 (1.228–2.187) | 0.0008 | 49 |
| Intake of whole-grain bread (each 50 g/day) | −0.085 | 0.918 (0.855–0.986) | 0.0193 | −9 |
| Consumption of coffee (each 150 g/day) | −0.043 | 0.958 (0.926–0.991) | 0.0142 | −4 |
| Moderate alcohol consumption (between 10 and 40 g/day) | −0.198 | 0.821 (0.705–0.954) | 0.0104 | −20 |
| Sports, biking, or gardening (h/week) | −0.016 | 0.984 (0.973–0.995) | 0.0060 | −2 |
| Former smoker | 0.237 | 1.267 (1.094–1.469) | 0.0016 | 24 |
| Current heavy smoker (≥20 cigarettes/day) | 0.642 | 1.901 (1.470–2.458) | <0.0001 | 64 |

of diabetes during the following 5 years based on the following formula:

$$P\,(diabetes) = 1 - h_0\,(t)^{exp(\text{score points}/100)}$$

We validated the predictive properties of the German Diabetes Risk Score in the EPIC-Heidelberg study cohort, using the same risk score measures as in the EPIC-Potsdam. To do so, we first estimated each subject's probability of developing diabetes based on the derived German Diabetes Risk Score. The proportion of incident cases observed within categories of estimated diabetes probability over a follow-up period of 5 years in the EPIC-Heidelberg study was then calculated.

We further validated the usefulness of the German Diabetes Risk Score to predict physiologic measures of insulin sensitivity and secretion among nondiabetic participants of the TÜF and the MeSyBePo studies. Data for food intake were available only in a minority of the participants in these studies. Thus, sex-specific population means from the EPIC-Potsdam were used to calculate the score values. Scatter plots and linear regression models were used to evaluate bivariate relationships between the German Diabetes Risk Score, insulin sensitivity, and the disposition index from the OGTT. Insulin sensitivity was calculated by the formula of Matsuda and DeFronzo (24). First-phase insulin release was calculated with the formula of Stumvoll et al. (25), and a disposition index was calculated by multiplying insulin sensitivity with insulin secretion (26).

We also evaluated the predictive power of the German Diabetes Risk Score to identify individuals at high risk of developing type 2 diabetes in the EPIC-Potsdam and the EPIC-Heidelberg studies and to identify individuals with undiagnosed diabetes in the TÜF and the MeSyBePo studies through receiver-operator characteristic (ROC) curve analysis (27) based on logistic regression models, with the area under the curve (AUC) being a measure of the predictive ability.

**RESULTS** — We defined one model from Cox regression consisting of waist circumference, height, age, a history of hypertension, red meat consumption, whole-grain bread consumption, coffee consumption, moderate alcohol drinking (10–40 g/day), physical activity, and smoking (former and current heavy) (Table 1). Models generating risk functions separately for men and women had similar β-coefficients and are not reported. β-Coefficients were used to assign points for each variable to the total German Diabetes Risk Score according to the following formula:

$$\begin{aligned}\textit{German Diabetes Risk Score} = {} & 7.4 \times \textit{waist}\,(\textit{cm}) \\ & - 2.4 \times \textit{height}\,(\textit{cm}) \\ & + 4.3 \times \textit{age}\,(\textit{years}) \\ & + 46 \times \textit{hypertension} \\ & + 49 \times \textit{red meat}\,(150\ \textit{g/day}) \\ & - 9 \times \textit{whole-grain bread}\,(50\ \textit{g/day}) \\ & - 4 \times \textit{coffee}\,(150\ \textit{g/day}) \\ & - 20 \times \textit{moderate alcohol} \\ & - 2 \times \textit{physical activity}\,(\textit{h/week}) \\ & + 24 \times \textit{former smoker} \\ & + 64 \times \textit{current heavy smoker}\end{aligned}$$

The probability (*P*) of developing diabetes during the following 5 years was calculated with the estimated baseline hazard function from the Cox model:

$$P\,(diabetes) = 1 - 0.999854^{exp(\text{score points}/100)}$$

The probability of developing diabetes in the EPIC-Potsdam for 300, 350, 400, 450, 500, 550, 600, 650, 700, and 750 points at the German Diabetes Risk Score were 0.3, 0.5, 0.8, 1.3, 2.1, 3.5, 5.7, 9.3, 14.8, and 23.2%, respectively. Sensitivity, specificity, and the predicted value of a positive test result were, respectively, 83.1, 68.3, and 5.9% at ≥500 score points, 67.5, 80.6, and 7.7% at ≥550 points, and 50.3, 89.9, and 10.7% at ≥600 points.

We estimated the diabetes probability for the German Diabetes Risk Score depending on age and waist circumference for a person with otherwise the following characteristics assumed: height 170 cm; never smoker; no alcohol consumption; no consumption of red meat, whole-grain bread, or coffee; no history of hypertension; and 0 h activity per week. The absolute risk to develop diabetes increased with both age and waist circumference, but the increase with age was small for individuals with small waist circumference (0.4% at age 35 and 1.7% at age 65 with waist = 80 cm), while diabetes risk was substantially higher at higher waist circumference even at lower age (7.7% at age 35 and 25.2% at age 65 for waist = 120 cm).

The estimated diabetes probability agreed well with the observed incidence in the EPIC-Potsdam (Table 2) study. We also estimated the diabetes probability in the EPIC-Heidelberg cohort and compared this with the observed incidence. In this independent cohort, the observed incidence lay within the range predicted. Similarly to the EPIC-Potsdam study, the observed incidence increased with increasing risk score points. Sensitivity and

**Table 2—*Diabetes incidence during follow-up of the first 5 years of the EPIC-Potsdam and the EPIC-Heidelberg studies by categories of the German Diabetes Risk Score***

| | | EPIC-Potsdam | | | EPIC-Heidelburg | | |
|---|---|---|---|---|---|---|---|
| Estimated probability (%) | Score | *N* | *n* | % | *N* | *n* | % |
| <1 | <423 | 11,055 | 18 | 0.2 | 9,303 | 30 | 0.3 |
| 1 to <2 | 423 to <493 | 5,337 | 69 | 1.3 | 4,909 | 65 | 1.3 |
| 2 to <3 | 493 to <534 | 2,725 | 75 | 2.8 | 2,662 | 53 | 2.0 |
| 3 to <5 | 534 to <586 | 2,689 | 104 | 3.9 | 2,781 | 134 | 4.8 |
| 5 to <10 | 586 to <658 | 2,215 | 147 | 6.6 | 2,397 | 171 | 7.1 |
| ≥10 | ≥658 | 1,146 | 176 | 15.4 | 1,346 | 205 | 15.2 |

specificity were 94.4 and 66.7% at ≥500 points and 79.7 and 79.3% at ≥550 points, respectively, in the EPIC-Heidelberg study. In both cohort studies, ROC curve analysis demonstrated that the German Diabetes Risk Score predicted incident type 2 diabetes very well (AUC 0.84 in the EPIC-Potsdam and 0.82 in the EPIC-Heidelberg study).

The associations between the German Diabetes Risk Score and measures of insulin sensitivity and secretion among nondiabetic participants in the TÜF and the MeSyBePo studies are shown in Fig. 1. In the TÜF study, correlation coefficients between the German Diabetes Risk Score and insulin sensitivity and disposition index were −0.56 and −0.44, respectively. Similarly, in the MeSyBePo study, correlation coefficients were −0.45 for insulin sensitivity and −0.36 for disposition index. ROC curve analyses also indicated good performance of the German Diabetes Risk Score in identifying participants who had undiagnosed diabetes in these studies (AUC 0.83 in the TÜF and 0.75 in the MeSyBePo study). The sensitivity and specificity of the German Diabetes Risk Score to identify undiagnosed diabetes at a cutoff of ≥500 points were 82.8 and 72.2% in the TÜF and 93.9 and 42.6% in the MeSyBePo study, respectively. The corresponding values at a cutoff of ≥550 points were 62.1 and 83.1% in the TÜF and 83.1 and 57.0% in the MeSyBePo study, respectively.

**CONCLUSIONS** — The German Diabetes Risk Score allows for accurately estimating the 5-year probability of developing diabetes in Caucasian study populations from Germany based on anthropometric, dietary, and lifestyle factors that predominantly represent modifiable risk factors of diabetes. It may therefore represent a useful screening tool for identification of high-risk individuals who would benefit from diet and lifestyle changes or medication such as acarbose or metformin. Furthermore, the German Diabetes Risk Score might be useful as a screening tool to identify undiagnosed diabetes.

We modeled waist circumference, which contributed strongly to our German Diabetes Risk Score, as a continuous variable to capture its full predictive information. This is in agreement with most

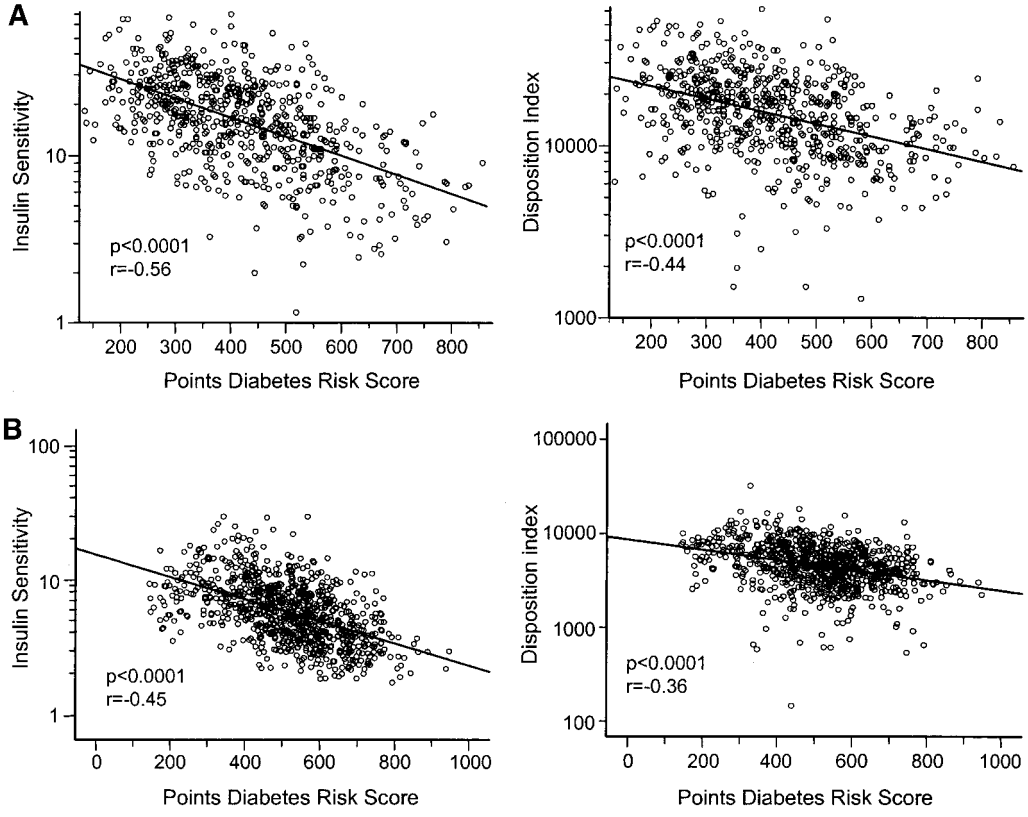


**Figure 1**—*Correlation between the German Diabetes Risk Score and insulin sensitivity (Matsuda and DeFronzo [ref. 24]) and disposition index (insulin sensitivity multiplied by first-phase insulin response) from the OGTT in the TÜF* (A) *and the MeSyBePo* (B) *studies.*

previous studies (6,8–10) on diabetes risk scores that aimed at identifying high-risk individuals except one (7), which used three categories only for BMI and waist circumference. It is well established that obesity is an important risk factor for type 2 diabetes, and randomized trials (1–4) have shown that weight reduction as the primary target of diet and lifestyle interventions can prevent or delay the development of type 2 diabetes. Also, it has previously been shown that physical activity and moderate alcohol consumption are inversely associated with diabetes risk, whereas smoking increases the risk of developing diabetes (28–31). There is also good evidence that consumption of red meat (32–35), whole-grains (36–39), and coffee (40) are associated with diabetes risk. Factors included in our German Diabetes Risk Score therefore represent established risk factors. Importantly, most factors are dietary and lifestyle factors, suggesting that their change substantially reduces the risk of developing type 2 diabetes. Although only the modifiable risk factors can be addressed by interventions, nonmodifiable risk factors like age are important components to determine an individual's risk and have previously been widely used in risk prediction models for diabetes (6–11) and other chronic diseases (41).

Incident cases in the EPIC studies were detected by routine medical examinations. Thus, the estimated 5-year diabetes probability reflects the probability of a diagnosis of diabetes according to the practice of diabetes screening and diagnosis in Germany at the time of the study. In contrast to our study, most previous studies that derived diabetes risk scores to identify high-risk individuals actively screened the study population for prevalent and incident diabetes using fasting glucose or an OGTT as diagnostic tools (6,8–10). The incidence of diabetes in these studies therefore reflects the incidence that could be expected if universal diabetes screening was common practice.

Only the Finrisk studies (7) and the ARIC study (9) relied exclusively on factors that are measurable with noninvasive methods. Similar to our study, the Finrisk studies are based on the physician's diagnosis of diabetes. However, the Finrisk studies considered only drug-treated diabetes as incident outcome. It did not identify incident cases treated by diet and lifestyle only and has therefore probably underestimated the incidence of diabetes in this cohort (7). Also, in contrast to our study, the study included prevalent diabetic participants without drug treatment at baseline. A recent analysis from the German Cooperative Health Research in the Region of Augsburg study suggests a low validity of the Finrisk score to identify undiagnosed diabetes in German study populations (ROC AUC 0.65) (12). With regard to the ARIC study (9), the observed validity to identify individuals who develop diabetes in the testing sample of this study (ROC AUC 0.71) was considerably lower compared with the performance of our score in the EPIC-Heidelberg study. The applicability of the ARIC risk score to European Caucasian populations may generally be limited because it was derived from a U.S. population comprising African Americans as well as Caucasians. The observed prediction of incident diabetes by the German Diabetes Risk Score was similar or better compared with previously published risk scores that relied on invasive measurements (6,8–10). Measures of insulin resistance and impaired insulin secretion, which are risk factors for type 2 diabetes (42,43), from the OGTT correlated well with the German Diabetes Risk Score in the TÜF and the MeSyBePo studies, further supporting the usefulness of the score.

It should be noted that self-reporting bias and random error in the measurement of score components may have limited our ability to obtain accurate risk estimates and may have led to an underestimation of the predictive strength of the score components. In particular, physical activity has not been validated with an objective measure like heart rate monitoring in the EPIC cohorts. Smoking and alcohol consumption are value-laden behaviors prone to underreporting. In addition, the applicability of the German Diabetes Risk Score in the TÜF and the MeSyBePo studies may have been limited by the different assessment instruments applied and by the lack of dietary information in most participants of these studies. However, in spite of these limitations the measurements and the deduced German Diabetes Risk Score performed similarly well in the two EPIC cohorts and predicted insulin resistance in two other cohorts with acceptable accuracy.

In conclusion, the German Diabetes Risk Score is an accurate tool for identifying individuals at high risk of developing type 2 diabetes in the general population. The score is publicly available as an interactive Web tool at the Web site of the German Institute of Human Nutrition (www.dife.de).

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