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2016

Barengo , N C & Tuomilehto , J O 2016 , ' How can we identify candidates at highest risk - to screen or not to screen? ' , Herz , vol. 41 , no. 3 , pp. 175-+ . <https://doi.org/10.1007/s00059-016-4417-5>

<http://hdl.handle.net/10138/223985>

<https://doi.org/10.1007/s00059-016-4417-5>

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Please cite the original version.

Herz 2016 · 41:175–183
 DOI 10.1007/s00059-016-4417-5
 Published online: 6 April 2016
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Introduction

The number of people living with type 2 diabetes mellitus (T2D) is growing rapidly. Currently, 415 million people worldwide have T2D and about 75 % live in low- or middle-income countries [1]. The overall number of people with T2D is expected to increase to about 642 million people in 2040. Moreover, it has been estimated that 12 % of global health expenditure is spent on diabetes, much of this due to multiple complications, in particular secondary and tertiary care of cardiovascular disease (CVD) [2]. T2D is associated with an increased risk of many co-morbidities compared with the rest of the population [3–6]. The risk of cardiac diseases, peripheral vascular disease and stroke is significantly higher in people with T2D compared with those without diabetes, and premature mortality caused by diabetes results in an estimated 12–14 years of life lost, representing a huge economic burden in many countries [3, 4]. It has been estimated that about 10–15 % of the total health care costs in developed countries are spent on treating diabetes, particularly its complications [7, 8].

Based on epidemiological observations, about half of the population will develop T2D during their lifetime, and up to 30–35 % will have impaired glucose tolerance (IGT) [9, 10]. Therefore, it is likely that more than half of the pop-

ulation carry genes that predispose to the development of T2D. Even though genetic effects are important for the development of the disease, it is not possible to modify them to prevent T2D. Dysglycemia is a progressive disorder; in people with IGT, approximately half develop T2D during a 10-year follow-up, and in Asian populations the rate of progression seems to be even faster [11–13]. It is important to understand that the risk of complications begins in the pre-diabetic phase, before blood glucose levels reach diagnostic cut-off points for, T2D resulting in significant morbidity and mortality from CVD [7, 14, 15]. With an increasing number of T2D patients worldwide, the number of patients with CVD will inevitably also rise. To avoid late complications of T2D and related costs, primary prevention of T2D itself and its early treatment are therefore necessary.

Why screen people at a high risk of T2D?

For disease prevention two approaches can be used: the population approach and the high-risk approach. The population approach does not require the identification of high-risk people, but preventive measures target the entire population, e.g. the promotion of physical activity. The high-risk approach starts with the identification of people at the high end of

the risk distribution. The most efficient strategy in prevention is obviously the combination of these two approaches.

Obesity, unbalanced diet and physical inactivity are the major risk factors for diabetes. In people genetically predisposed to the disease, the probability of developing T2D is very high once exposed to unhealthy lifestyles. Fortunately, current scientific evidence from randomized controlled trials has revealed that the progression to T2D can be prevented or delayed in people with IGT by lifestyle intervention (■ Tab. 1, [12, 13, 16–20]). The Finnish Diabetes Prevention Study (DPS) revealed that individualized counselling aimed at reducing weight, total intake of fat, and intake of saturated fat and increasing intake of fiber and physical activity, the risk of diabetes can be reduced by up to 58 % compared with people with IGT who do not undergo any intervention [16]. A 6-year diet and exercise intervention was carried out in a cluster-randomized trial in Da-Qing, China, in 577 participants (mean age 45.0 years, mean BMI 25.8) with IGT were assigned either to the control, exercise alone, diet alone, or exercise plus diet groups [12]. The cumulative 6-year incidence of T2D was lower in each of the three intervention groups compared with the control group; the relative risk reduction in incidence was approximately 40 % during the 6-year intervention period. The US Diabetes Prevention Program (DPP) ran-

Tab. 1 Summary of lifestyle intervention trials in people with glucose metabolism disorders

Author, year	Country	Number of participants	Intervention	Follow-up (years)	Risk reduction of lifestyle modification (%)
Pan et al., 1997 [12]	China	530	Diet, physical activity	6	42
Tuomilehto et al., 2001 [16]	Finland	522	Diet, physical activity	3.2	58
Knowler et al., 2002 [17]	USA	5234	Diet, physical activity, metformin	2.8	58
Kosaka et al., 2005 [18]	Japan	458	Diet, physical activity	4	67
Ramachandran et al., 2006 [13]	India	531	Diet, physical activity, metformin	2.5	29
Roumen et al., 2008 [19]	The Netherlands	147	Diet, physical activity	3	58
Penn et al., 2009 [20]	United Kingdom	102	Diet, physical activity	3.1	55
Saito et al., 2011 [24]	Japan	641	Diet, physical activity	3	44

domized people with IGT and fasting glucose ≥ 95 mg/dl to receive intensive dietary and exercise counselling, metformin, or placebo [17]. The relative risk reduction after 2.8 years of follow-up in the lifestyle intervention group compared with the placebo control group was 58 %, similar to the results from the DPS. The effect of lifestyle intervention was superior to that of metformin treatment, which showed a 35 % relative risk reduction. Other studies such as the Indian DPP and the Japanese IT intervention trial revealed similar findings to those in the above-mentioned studies. All in all, the reduction in T2D incidence in those trials varied between 29 % and 67 %.

Lifestyle intervention in people with IGT during 4 years in the DPS induced sustaining lifestyle change and resulted in the long-term prevention of progression to type 2 diabetes (hazards ratio of T2D 0.61 compared with the initial control group) [21]. Moreover, the absolute risk reduction seemed to increase even after the actual lifestyle intervention program was ceased. Also, the participants with IGT who received a 6-year lifestyle intervention in the Chinese Da Qing study had a statistically significantly lower incidence of T2D two decades later com-

pared with people of the control group [22]. During the 10-year overall follow-up of the US DPP Outcomes Study, the incidence of T2D in the original lifestyle intervention group remained lower than in the control group [23]. Thus, all three long-term follow-up studies of the clinical lifestyle intervention trials showed that adherence to lifestyle changes during the intervention period predicted a greater risk reduction during the total follow-up. It was estimated that lifestyle intervention needs to be provided for 6.4 high-risk individuals for an average of 3 years to prevent 1 case of diabetes.

At present, there are limited data to show whether progression from impaired fasting glucose (IFG) to T2D can be stopped by lifestyle intervention. The only clinical lifestyle trial that recruited people with IFG demonstrated a 59 % relative risk reduction in people who had IFG and IGT combined, but failed to show any benefit with regard to T2D incidence in people who only had IFG [24]. Thus, there is convincing scientific evidence that treatment after early detection in people with IGT yields benefits superior to those obtained when treatment is delayed; T2D can be successfully prevented or its onset delayed in people

with IGT, at least in a well-controlled clinical setting [24].

Considering the evidence presented above, it is important to identify people at a high risk of T2D, as they will benefit from early lifestyle changes with regard to the future development of T2D. Plasma glucose (fasting or 2 h after the Oral Glucose Tolerance Test, OGTT) and HbA1c testing are recommended methods for the diagnosis of T2D in the general population [25]. However, these are invasive, expensive and time-consuming procedures (especially the OGTT), and are hence not suitable as mass screening activities. Moreover, it has been commonly agreed that the detection of blood glucose at random in the population is not justified because glucose levels in the blood are highly variable [26]. The US recommendations have emphasized that fasting blood glucose may be less variable and more useful for screening purposes [25]. However, it has been revealed that the vast majority of early cases of asymptomatic T2D and IGT would not be detected by measuring fasting glucose alone [27, 28]. Therefore, a simple, rapid, and non-invasive score for identifying high-risk subjects is needed in primary care. A screening test is usually not diagnostic in itself, but in most cases is followed by appropriate invasive diagnostic tests to confirm the results. The screening process starts by selecting the target population, followed by a screening test to divide individuals into either apparently healthy or at-risk. For the apparently healthy individuals, regular screening at fixed relaxed 5- to 10-year intervals is recommended. The at-risk people are referred for further evaluation and subsequent diagnostic, usually laboratory, investigations. Appropriate intervention is started among those with a confirmed risk status to reduce the risk of progression to T2D.

Several non-invasive tests have been developed as screening tools to assess the risk of T2D and to detect undiagnosed T2D. These include the American Diabetes Association (ADA) Risk Tools, the Finnish Diabetes Risk Score (FIND-RISC), the National Health and Nutrition Examination Survey (NHANES) Risk Score, the Australian Diabetes Risk

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Score [29–38]. The Finnish Diabetes Risk Score (FINDRISC) is probably one of the most efficient screening tools. It is based on easily available information using eight parameters with categorized answers about age, body mass index (BMI), waist circumference, physical activity, daily consumption of fruit and vegetables, a history of antihypertensive drug treatment, a history of high blood glucose, and a family history of diabetes [29]. The total risk score value ranges from 0 to 26. The FINDRISC was shown to predict the 10-year risk of drug-treated T2D with a sensitivity of 78–81 % and a specificity of 76–77 %. Furthermore, it detects prevalent asymptomatic T2D and other glucose metabolism disorders reasonably efficiently [39]. The FINDRISC was first validated in Italian and Greek populations with identical results [40, 41], was successfully applied in primary care in Barcelona, Spain [42], and was recommended in the guideline by the European Society for the Study of Diabetes and the European Society of Cardiology as a screening tool for T2D [43]. Recently, a European study validating existing non-laboratory-based models and assessing the variability in predictive performance in European populations found that existing diabetes prediction models can be used to identify individuals at a high risk of T2D in the general population [44]. Thus, screening tests for identifying people at a high risk of T2D are available and can detect the preclinical stage of the disease.

Almost 40 years ago, Wilson and Jungner attempted to define screening criteria to guide the selection of conditions that would be suitable for screening, based, among other factors, on the capacity to detect the condition at an early stage and the availability of an acceptable treatment [45]. They proposed that seven conditions have to be met to justify screening tests. In the case of screening for people at a high risk of T2D, there is convincing scientific evidence that screening for T2D fulfils the first five criteria proposed by Wilson and Jungner.

Herz 2016 · 41:175–183 DOI 10.1007/s00059-016-4417-5
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Abstract

Type 2 diabetes (T2D) causes a large economic and health-care burden globally. This article summarizes the benefits and unsolved questions of screening for T2D. Many T2D risk assessment tools have been developed. Furthermore, current evidence has shown that T2D can be prevented by lifestyle interventions, justifying T2D screening. However, information is scarce on the long-term impact of T2D screening regarding health outcomes such as cardiovascular disease. Moreover, it is not certain whether health-care facilities and health-care staff are capable of implementing screening activities and subsequent interventions among high-

risk individuals; lifestyle management tasks in particular are often not among the best skills that health-care personnel possess. Also, there is a lack of evidence for the periodicity of population-wide screening activities. As national health-care systems increasingly implement T2D screening, we may receive in the near future answers to some of our remaining research questions to fully assess the benefits and disadvantages of screening.

Keywords

Screening · Type 2 diabetes · Harms · Advantages · Disadvantages

Wie können wir Personen mit dem höchsten Diabetesrisiko identifizieren – screenen oder nicht screenen?

Zusammenfassung

Typ-2-Diabetes (T2D) ist eine große Belastung für die Wirtschaft und die Gesundheitssysteme weltweit. Dieser Artikel fasst die Vorteile und die ungelösten Fragen zum Screenen nach T2D zusammen. Bisher sind viele T2D-Risikobewertungsinstrumente entwickelt worden. Darüber hinaus haben aktuelle Forschungsergebnisse gezeigt, dass T2D durch Änderungen im Lebensstil vermieden werden kann, was das T2D-Screening im Prinzip rechtfertigt. Allerdings gibt es kaum Informationen über die langfristigen Auswirkungen des T2D-Screenings in Bezug auf gesundheitliche Auswirkungen, z. B. auf kardiovaskuläre Erkrankungen. Außerdem ist unklar, ob Gesundheitseinrichtungen und -personal in der Lage sind, die Screeningaktivitäten

und die Folgemaßnahmen bei Personen mit hohem T2D-Risiko umzusetzen. Insbesondere Eingriffe in den Lebensstil zählen nicht zu den vorrangigen Aufgaben des Personals im Gesundheitswesen. Außerdem gibt es bislang nur ungenügende Dokumentationen hinsichtlich der Regelmäßigkeit der bevölkerungsweiten T2D-Screeningaktivitäten. Da nationale Gesundheitssysteme vermehrt auf T2D-Screenings setzen, werden wir wohl in naher Zukunft Antworten auf einige verbleibende Forschungsfragen erhalten, um die Vor- und Nachteile des Screenings vollständig beurteilen zu können.

Schlüsselwörter

Typ-2-Diabetes · Vorteile · Identifizierung · Lebensstil · Interventionen

Unsolved questions related to T2D screening

One of the main current debates is related to which invasive screening test to use as the second step after non-invasive risk score in the T2D risk assessment. The classification of diabetes and other disorders of glucose metabolism are based on the definitions of the World Health Organization (WHO) [25, 46] and the American Diabetes Association

(ADA) [47]. There is some disagreement with regard to recommended diagnostic tests between the WHO and ADA (■ Tab. 2). Although the ADA backs the use of HbA1c as the primary diagnostic test for diabetes mellitus (DM) [47], the WHO uniquely recommends an OGTT [46, 48]. The OGTT is considered to be the gold standard test for screening and diagnosis [46, 48], as it takes into account both fasting and post-prandial glucose abnormalities. A standardized

Tab. 2 Comparison of the diagnostic criteria for diabetes mellitus between the World Health Organization (WHO) and the American Diabetes Association (ADA)					
	Test	WHO		ADA	
Diabetes	HbA1c	Not recommended		≥ 6.5 %	(48 mmol/l)
	FPG	≥ 7.0 mmol/l	(≥ 126 mg/dl)	≥ 7.0 mmol/l	(≥ 126 mg/dl)
	2hPG	≥ 11.1 mmol/l	(≥ 200 mg/dl)	≥ 11.1 mmol/l	(≥ 200 mg/dl)
Impaired glucose tolerance	FPG	< 7.0 mmol/l	(< 126 mg/dl)	< 7.0 mmol/l	(< 126 mg/dl)
	or 2hPG	≥ 7.8– < 11.1 mmol/l	(≥ 140– < 200 mg/dl)	Not required	
Impaired fasting glucose	FPG	6.1–6.9 mmol/l	(110–125 mg/dl)	5.6–6.9 mmol/l	(100–125 mg/dl)
	or 2hPG	< 7.8 mmol/l	(< 140 mg/dl)	Not required	

FPG fasting plasma glucose, *2hPG* 2-h post-load plasma glucose

OGTT is performed in the morning after an overnight fast (8–14 h). One blood sample should be taken before, and one 120 min after intake of 75 g of glucose dissolved in 250–300 ml of water for 5 min (note that the timing of the test begins when the patient starts to drink).

The 2-h plasma glucose test in an OGTT provides a sensitivity of 97 %, with a specificity of 100 % [49]. To diagnose DM, a confirmatory laboratory glycemic test (FPG, casual PG, HbA1c or 2hPG in a 75-g OGTT) is necessary on another day in all cases in the absence of unequivocal hyperglycemia accompanied by acute metabolic decompensation. Repeat confirmatory testing on another day may be considered in the absence of symptoms. The HbA1c test, on the other hand, provides a retrospective average of glycemic control for the previous 3 months, by measuring the binding glucose to hemoglobin during the life span of red blood cells. A blood sample is easy to collect, as the HbA1c test does not require individuals to fast and there is practically no diurnal variation in HbA1c. In an analysis of three ethnically varied US databases, the proposed ADA diagnostic criteria for diabetes (HbA1c ≥ 6.5 %) failed to detect 70 % of individuals with diabetes and 71–94 % with abnormal glucose tolerance. However, the HbA1c resulted in more normal diagnoses than the OGTT [50]. A study conducted in a Spanish population [51] revealed that defining diabetes by a single HbA1c measurement resulted in a dramatic decrease in DM prevalence (1.3 %),

particularly in comparison with diabetes defined by 2hPG (8.6 %), but was also significant with regard to FPG (2.8 %). In the DPS the sensitivity of the HbA1c ≥ 6.5 % (≥ 48 mmol/mol) as a diagnostic criterion for T2D was 35 % (95 % CI 24–47 %) in women and 47 % (95 % CI 31–64 %) in men, compared with diagnosis based on two consecutive OGTTs [52]. Of those with T2D diagnosis based on two OGTTs during the DPS follow-up, 60 % would have remained undiagnosed if diagnosis had been based on the HbA1c ≥ 6.5 % (≥ 48 mmol/mol) criterion.

In summary, the main problem with the HbA1c is that it has a low sensitivity in predicting DM, as it is a secondary phenomenon after high glucose in blood circulation. Thus, HbA1c values < 6.5 % do not exclude DM that may be detected by FPG or 2hPG [48, 50–52]. Thus, the diagnosis will be delayed. It is important to mention that the diagnosis of DM or abnormal glucose tolerance depends on whether FPG is measured alone or combined with a 2hPG value of an OGTT [53]. A normal FPG reflects an ability to maintain adequate basal insulin secretion in combination with hepatic insulin sensitivity sufficient to control hepatic glucose output. A post-load glucose level within the normal range requires an appropriate insulin secretory response and adequate insulin sensitivity in peripheral tissues. Thus, an individual with IFG in the fasting state may have undetected IGT or even DM. The usual argument in favor of a FPG or an HbA1c over a 2hPG is primarily related to feasibility

or practicability and not scientific evidence. The WHO criteria are based on fasting plasma glucose (FPG) and 2hPG concentrations, and recommend the use of an OGTT in the absence of overt hyperglycemia [46, 48]. The ADA criteria encourage the use of HbA1c, fasting glycaemia, and, as a third option, possibly OGTT [47]. Recently, the EUROASPIRE IV, a cross-sectional survey in 24 European countries of patients ($n = 4,004$) aged 18–80 years with coronary artery disease, but with no reported history of diabetes, revealed that in patients with established coronary artery disease the OGTT identifies the largest number of patients with previously undiagnosed diabetes and should be the preferred test when assessing the glycemic state of such patients [54].

It is commonly agreed that there is no perfect diagnostic test for T2D. Although the OGTT is inconvenient and time-consuming, requires overnight fasting and its social acceptance may be poor, the fasting blood glucose test lacks sensitivity. So does HbA1c testing, which costs more than simple plasma glucose measurement and will miss many people who are identified as diabetic by an OGTT. Therefore, HbA1c cannot be applied in a large part of the world. The advantages and disadvantages of the HbA1c and the OGTT are presented in [Tab. 3](#).

Another unsolved issue is to define the optimal time interval between screening activities. Very little scientific information is available on the appropriate frequency of screening [55, 56]. The optimal interval between screening examinations is the one at which the prevalence of undiagnosed cases reaches the prevalence of such cases at the previous screening, and the cost-effectiveness is the same for each screening effort [57]. Davies et al. studied whether a screening program for diabetes repeated after an interval of 30 months in 3,200 patients registered at a general clinic is worthwhile, both in terms of yield of new cases and continued high response rate [55]. The repeat screening response rate was somewhat lower than the initial response rate (73 vs. 79 %). Furthermore, little information is available regarding the attendance for an OGTT after a positive screening test. Although Davies et

Tab. 3 Advantages and disadvantages of assays for glucose and HbA1c testing. (Adapted from [48])

	Glucose	HbA1c
Patient preparation before collection of blood	Stringent requirements if measured for diagnostic purposes	None
Processing of blood	Stringent requirements for rapid processing, separation and storage of plasma or serum at a minimum of 4 °C	Avoid conditions for more than 12 h at temperatures > 23 °C. Otherwise keep at 4 °C (stability for a minimum of 1 week)
Measurement	Widely available	Not readily available worldwide
Standardization	Standardized to reference method procedures	Standardized to reference method procedures
Routine calibration	Adequate	Adequate
Interferences: illness	Severe illness may increase glucose concentration	Severe illness may shorten red-cell life and artifactually reduce HbA1c values
Hemoglobinopathies	Few problems unless the patient is ill	May interfere with measurement in some assays
Hemoglobinopathy traits	No problems	Most assays are not affected
Affordability	Affordable in most low- and middle-income country settings	Unaffordable in most low- and middle-income country settings

al. reported compliance of 93 % following a positive screening test, only approximately half of the high-risk individuals invited to an OGTT turned up at the laboratory in the DEMOJUAN project in Colombia [56]. The reasons may be partly related to a time constraint, as the test requires attendance at the laboratory in the morning and takes at least 2 h, which may be difficult to arrange for people working during the daytime. Thus, it is a future challenge to develop a strategy to motivate people identified as being at a high risk of T2D to attend the diagnostic laboratory test. Novel strategies, such as a recently developed home-based OGTT test, may improve compliance [58].

Several questions remain to be answered, for instance, as to how to ensure periodic screening, how often screening should occur, and the frequency of attendance for a laboratory test followed by a positive screening test.

It would be very useful to have information on the long-term benefits of T2D screening programs. However, only little information is available [59, 60]. In the only real diabetes screening study, the ADDITION (Anglo-Danish-Dutch study of intensive treatment in people with screen detected diabetes in primary care) trial, one-third of the practice population, aged 40 to 65 years, was screened by an OGTT between 1990 and 1992

[60]. The study participants were thereafter invited for repeat screening during 1994–1996 and 2000–2002. The other two-thirds of the study population were not initially followed up, but a randomly selected subsample (50 %) was invited for diabetes screening between 2000 and 2002. The general practitioners were informed of the screening results and were free to apply whatever treatment they considered appropriate. This study revealed after 13-year follow-up that there were no differences in cardiovascular outcomes or self-reported health status. The ADDITION-Cambridge trial was not a screening trial, but compared intensive intervention with standard care in people found to have undiagnosed diabetes by screening [59]. Uptake was lower if people had to have OGTTs, or if screening involved blood tests on more than one visit. However, they found that the uptake of blood glucose testing was improved if people were made aware in advance that they were at a high risk. However, after 10 years of follow-up, there was no reduction in cardiovascular, diabetes-related or total mortality events between the intervention group and the control group. It has been suggested that these results might be explained by improvements in standard care, especially as the treatment effect of blood pressure and cholesterol levels in the standard-

care arm were similar to those in the intervention arm.

Any study assessing the long-term benefits of screening needs to be checked for lead-time bias. If it is possible to diagnose T2D earlier, but not to improve survival after diagnosis, the screening program will have an over-representation of earlier diagnosed patients, whose survival will be increased by exactly the amount of time their diagnosis was advanced by the screening program. If no intervention is provided in cases identified by a screening program, individuals will live exactly as long as they would without the screening program. Thus, a screening program that does not provide interventions for those at a high risk does not make much sense at all and may be even unethical. With regard to cost-effectiveness, a systematic literature review pointed out that screening for T2D and IGT, with appropriate intervention for those with IGT in an above-average-risk population aged 45, seems to be cost effective [61]. However, the cost-effectiveness of a policy of screening for diabetes alone, which offered no intervention to those with IGT, is still uncertain.

Only a few studies have studied the short- or long-term impact of diabetes screening programs. Studies assessing the long-term consequences of a diabetes screening program on psychological harms agree that there is no significant impact on anxiety, depression or quality-of-life subscales [62–69]. A recent study including 15 practices (10 screening, 5 controls) in the ADDITION-Cambridge trial in the east of England recruited 7,380 adults (aged 40–69) in the top fourth for risk of having undiagnosed T2D [62]. To our knowledge, this is the only trial to include a control group at a similar risk of having undiagnosed T2D. They found no significant differences in any of the five outcome measures (state anxiety, anxiety, depression, diabetes-specific worry, and self-rated health) between the screening attenders and control participants at the initial random blood glucose test, or between those invited for screening and controls at 3–6 months and 12–15 months. These results are in line with a recent meta-analysis of 12 studies,

which revealed no significant impact on longer term anxiety, depression or quality-of-life subscales [70].

Only a few studies exist on the short-term emotional impact of screening [63, 71]. In a randomized controlled trial in two general practices in the UK, people at a high risk of having undiagnosed T2D were assigned to either an invited or a non-invited group [63]. Six weeks after the last contact (either test or invitation), a questionnaire was sent to all participants, including those who were not originally invited, assessing attendance, anxiety, self-rated health and diabetes illness perceptions. Invited participants were more anxious than those who had not been invited and those diagnosed with diabetes were considerably more anxious than those classified as being free of diabetes. Furthermore, non-attenders had a lower mean emotional representation sub-scale than attenders. Thus, predicting an individual's risk of illness seemed to be associated with an increase in short-term anxiety and depression [71].

Another important question in T2D screening is whether people diagnosed as being at a high risk of T2D are more likely to change their lifestyle than people who are unaware of their risk or whether a negative test may have an adverse shift in health behaviors. Results from the Cambridge MRC group found that screening for T2D is unlikely to cause an adverse shift in the population distribution of plasma glucose and cardiovascular risk, following an increase in unhealthy behaviors arising from false reassurance among people who have a negative screening outcome [72]. Moreover, the Hoorn study showed that the group with high-risk scores, but who did not have diabetes on glucose testing, had a risk of CVD almost as high as that in individuals who were glycaemia-positive, proposing that it might be of greater public health benefit to intervene in the entire screen-positive group than only in the relatively small group with increased glucose concentration in the subsequent laboratory tests [73].

Conclusions

T2D is inflicting a large economic burden on health-care systems all around the world. Considering that validated and low-cost T2D risk assessment tools exist, and that the current evidence has shown that T2D can be prevented by lifestyle interventions, T2D screening in the population may be justified. However, future studies need to assess the long-term impact of T2D screening on health outcomes such as CVD and psycho-neurological effects. Moreover, no information is available regarding the readiness and the capacity of the health-care facilities and health-care staff to implement screening activities and subsequent interventions among high-risk individuals. After all, lifestyle modifications are not usually included in the tasks of health-care personnel. People who are at a high risk must themselves make necessary lifestyle changes, and there are other people outside the traditional health sector who may be able to help them with issues of healthy diet and physical activity. Also, there is a lack of evidence on the periodicity of population-wide screening activities. As more and more national health-care systems are implementing T2D screening activities, we may in the near future receive answers to some of the remaining research questions to fully assess the benefits and disadvantages of screening.

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Compliance with ethical guidelines

Conflicts of interest. N. C. Barengo and J. O. Tuomilehto state that there are no conflicts of interest.

The accompanying manuscript does not include studies on humans or animals.

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Hirntod

Seit Juli 2015 gelten für die Hirntoddiagnostik die neuen Richtlinien der Bundesärztekammer in ihrer 4. Fortschreibung. Der Focus der

Zeitschrift *Der Nervenarzt* wurde daher in der Ausgabe 02/2016 auf den Schwerpunkt „Hirntod“ gerichtet. Sie erhalten Informationen über die neuen Richtlinien und einen Überblick über den Stand der Diskussion zu diesem sensiblen Thema, das für alle Ärzte bei der Arbeit im Klinikalltag eine wichtige Rolle spielt.

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- EEG und Evozierte Potentiale zum Irreversibilitätsnachweis der klinischen Ausfallssymptome des Gehirns
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gebung ist das Zeitmanagement absolut notwendig.

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