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Why screening for type 2 diabetes is necessary even in poor resource settings

Ranjit Unnikrishnan, Viswanathan Mohan *

Dr. Mohan's Diabetes Specialities Centre & Madras Diabetes Research Foundation, WHO Collaborating Centre for Non-communicable Diseases Prevention and Control, IDF Centre of Education, Gopalapuram, Chennai, India

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ABSTRACT

Screening for type 2 diabetes (T2DM) remains controversial, in spite of the explosive increase in the prevalence of the disorder and the morbidity and mortality associated with its complications. In this review, we attempt to show that T2DM is an ideal candidate disease for screening, and why screening is needed to improve clinical outcomes and prevent complications. We also suggest that screening can be made more cost-effective by adopting a targeted approach and utilizing low-cost tools. We conclude that screening for T2DM is warranted even in resource-constrained settings, and provide examples from rural India showing that such an approach is feasible with meticulous planning and judicious allocation of resources.

In medicine, screening is defined as a strategy by which individuals living in a defined population are offered a diagnostic test, in order to identify hitherto unrecognized disease. To be considered viable, appropriate and effective, a screening program should fulfill certain criteria, the most widely accepted of which have been suggested by Wilson & Jungner (1968) and subsequently adopted by the World Health Organisation. In brief, these criteria state that a screening program is justifiable, if:

1. The condition sought is an important health problem.
2. There is an accepted treatment for patients with recognized disease.
3. Facilities for diagnosis and treatment are available.
4. There is a recognizable latent or early symptomatic stage.
5. There is a suitable test or examination.
6. The test is acceptable to the population.
7. The natural history of the condition, including development from latent to declared disease, is adequately understood.
8. There is an agreed policy on whom to treat as patients.
9. The cost of case-finding (including diagnosis and treatment of patients diagnosed) is economically balanced in relation to possible expenditure on medical care as a whole.
10. Case-finding is a continuing process and not a "once and for all" project.

Screening protocols for certain conditions (such as cervical cancer) have gained wide acceptance and are now offered on a large scale in many countries, the benefits clearly outweighing the risks. However, there are certain other conditions for which screening is yet to gain universal acceptance. Type 2 diabetes mellitus (T2DM) is an example of such a condition.

In this article, we attempt to justify why screening for T2DM is justified and to show that after screening, subsequent management of those detected to have diabetes can be carried out even in resource-constrained parts of the world, using rural India as an example.

1. Diabetes is an ideal candidate for screening

The prevalence of T2DM is rapidly rising worldwide. The International Diabetes Federation (IDF) estimates that more than 382 million individuals have diabetes as of 2013 and this number is expected to rise to 592 million by 2030 (International Diabetes Federation, 2013). The largest numbers of individuals with diabetes reside in low and middle-income countries, where resources to treat the disease and its complications are admittedly scarce. Diabetes is the leading cause of end stage renal disease and non-traumatic lower extremity amputation worldwide. It ranks among the leading causes of preventable blindness and is a major modifiable risk factor for coronary artery disease and stroke.

The natural history of T2DM is relatively well-understood. It is known that in the majority of cases, frank diabetes is preceded by stages of "intermediate hyperglycemia" or "pre-diabetes" which, while asymptomatic, are associated with an increased risk of

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* Corresponding author at: Madras Diabetes Research Foundation & Dr. Mohan's Diabetes Specialities Centre, WHO Collaborating Centre For Non-Communicable Diseases Prevention and Control & IDF Centre of Education 4, Conran Smith Road, Gopalapuram, Chennai, 600 086, India. Tel.: +91 44 4396 8888; fax: +91 44 2835 0935.
E-mail address: drmohans@diabetes.ind.in (V. Mohan).

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progression to diabetes as well as of cardiovascular disease (Barr et al., 2007; Nathan et al., 2007; Tabák, Herder, Rathmann, Brunner, & Kivimäki, 2012). Interventions in the form of lifestyle modification as well as medications have been shown to significantly reduce the risk of progression of these intermediate stages to diabetes (Knowler et al., 2002; Tuomilehto et al., 2001). However, for such interventions to be instituted, individuals with "pre-diabetes" need to be identified sufficiently early on in the course of the disease; this is only possible through screening, as individuals in the stage of prediabetes are almost always asymptomatic.

There are a number of commonly used and widely accepted diagnostic tests for diabetes that are simple to perform, acceptable to the vast majority of the population, and in most cases, inexpensive. Well-defined treatment protocols have been put forth by various national and international organizations defining the thresholds for initiating treatment as well as the targets of such treatment (Garber et al., 2013; Inzucchi et al., 2012). Therefore, one has the option of choosing the most appropriate screening tool as well as treatment modality, depending on the clinical situation and the availability of resources.

The results of large randomized controlled trials have shown that tight control of diabetes, aiming for a glycated hemoglobin (HbA1c) level of 7% or below, can lead to significant reduction in the incidence and progression of microvascular complications of T2DM such as retinopathy and nephropathy (Ohkubo et al., 1995; UK Prospective Diabetes Study Group, 1998). The importance of early detection of diabetes and initiation of treatment has been established from the results of the United Kingdom Prospective Diabetes Study (UKPDS) follow-up, in which individuals with T2DM of relatively short duration initially randomized to intensive control of hyperglycemia, continued to derive the benefit of this intervention in the form of significantly reduced rates of cardiovascular disease and microvascular complications for up to 10 years after study completion, notwithstanding a deterioration in their HbA1c levels after termination of the initial intervention. This long-lasting effect of early tight glycemic control on development of chronic complications has been termed the "legacy effect" (Holman, Paul, Bethel, Matthews, & Neil, 2008). Unfortunately, since T2DM and the early stages of many of its complications tend to be silent, patients often come to the clinic only after they have developed complications of diabetes. Attempting tight glycemic control at this late stage of the disease does not seem to have similar protective effects to treatment initiated earlier on and, indeed, may be harmful (The Action to Control Cardiovascular Risk in Diabetes Study Group, 2008). Early detection of diabetes through screening programs thus enables the individual to build up a 'favorable' legacy effect through earlier initiation of effective treatment.

An individual's risk of developing diabetes complications depends largely on the magnitude of the "glycemic burden" to which one's cells are exposed during one's lifetime. We have recently shown that those who come for regular follow up to a diabetes centre accumulate much less glycemic burden and have a lower incidence of retinopathy and nephropathy compared to those who had irregular follow up at the centre (Anjana et al., 2015). Not surprisingly, therefore, much attention is being paid to reducing the "avoidable" glycemic burden i.e, the burden accumulated after the patient comes to medical attention, usually on account of "clinical inertia" on the part of the physician (Brown, Nichols, & Perry, 2004). However, there is also an "unavoidable" component to the glycemic burden; this is the burden accumulated before the patient is diagnosed with diabetes or before effective treatment is initiated. With earlier diagnosis of diabetes through effective screening programs, the "unavoidable" glycemic burden can also be minimized to a great extent (Fig. 1).

Diabetes and its complications are associated with enormous costs to the affected individual, his family and the society. It has been shown that an individual with diabetes in India spends more than Rs. 25,000 an year (USD 400 approx.) for management of his or her condition as of 2010, most of it (~80%) being 'out of pocket' expenditure (Tharkar, Devarajan, Kumpatla, & Viswanathan, 2010). When one considers that the per capita income of an average Indian during the same year was only Rs. 44,000 (USD 700 approx.), the magnitude of the economic burden due to diabetes becomes all too readily evident. Worse still, when an individual develops a complication such as a foot ulcer, it is estimated that the cost of care escalates to nearly 5.7 times the average annual income (Cavanagh et al., 2012). It is therefore reasonable to assume that by detecting diabetes early through inexpensive and easily available techniques and by instituting effective treatment, the excess burden due to diabetes complications can be prevented. Screening high-risk individuals for diabetes has been found to be cost-effective both in the short term as well as in the long run (Chatterjee et al., 2013; Hoerger et al., 2004), although admittedly more studies are needed, especially from low and middle income countries.

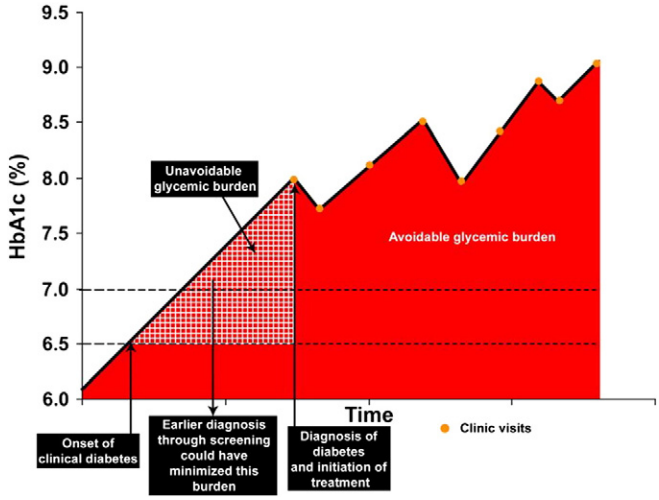

Fig. 1. Avoidable and unavoidable glycemic burden in type 2 diabetes.

2. Can screening be made more cost-effective?

In small, geographically discrete populations with high prevalence of diabetes (such as the Pima Indians and certain Pacific Islander populations), it would be appropriate, as well as feasible, to screen the entire population. However, in larger populations, it would be more cost-effective to target screening programs to those deemed to be at the highest risk of having diabetes. A number of "diabetes risk scores" have been devised in various populations to identify these individuals (Noble, Mathur, Dent, Meads, & Greenhalgh, 2011). Most of these risk scores utilize anthropometric parameters as well as demographic data in order to arrive at a composite score that indicates the individual's risk of developing diabetes. Screening using blood tests then needs to be carried out only in individuals who obtain scores indicating a high probability of diabetes. A couple of risk scores have also been devised for use in the Asian Indian population (Mohan, Deepa, Deepa, Somannavar, & Datta, 2005; Ramachandran, Snehalatha, Vijay, Wareham, & Colagiuri, 2005).

While the fasting plasma glucose, oral glucose tolerance test, random blood glucose and HbA1c are the accepted modalities for diagnosis of diabetes, their use may present certain difficulties and (in the case of OGTT and HbA1c) add considerably to the cost and logistics of the screening program in terms of availability of trained personnel and standardized laboratories. In resource-strapped settings, therefore, the random capillary blood glucose (RCBG) can be used as an initial step for opportunistic screening to identify those individuals who may require definitive testing. A RCBG value of 140 mg/dl (7.8 mmol/l) has been shown to identify those individuals likely to have diabetes with optimal sensitivity and specificity; the corresponding figure for "pre-diabetes" is 110 mg/dl (6.1 mmol/l)