EDITORIAL (SEE RITCHIE ET AL., P. 44)

Early Identification of Type 2 Diabetes

Policy should be aligned with health systems strengthening

More than 60% of the estimated 285 million people with diabetes globally are in low- and middle-income countries (LMICs) (1). Largely driven by the growth of type 2 diabetes, the numbers of people with diabetes worldwide is projected to touch at least 450 million by 2030, with the biggest increase happening in LMICs and substantially driven by populous Asian countries like India and China (1). Recent data indicate an urban diabetes age-standardized prevalence of 11.4% in China (2) and 9.1–13.0% in India in the ongoing Indian Council of Medical Research–India Diabetes (ICMR–INDIAB) study (V.M. Anjana, A. Mohan, personal communication). Furthermore, the prevalence of diabetes may be as high as 8.2% among rural residents in China (2) and may vary from 2.8 to 11.9% in rural India, depending on the level of economic development (ICMR–INDIAB study). Importantly, a high proportion of people with type 2 diabetes (50–70% in China [2,3] and 30–80% in India [ICMR–INDIAB study]) remain undiagnosed and thus untreated. Should there, therefore, be an active policy to identify dysglycemia and diabetes early?

As undiagnosed diabetes is frequently associated with potentially preventable costly diabetes complications and concomitant cardiovascular risk factors (4–6), a policy of early identification through systematic or opportunistic means may have some appeal. Indeed, the merits or otherwise of a screening policy for diabetes have been previously reviewed and assessed (7). The consensus thus far has been that type 2 diabetes meets many of criteria for screening, namely, the burden is large, the natural history is well understood, there is a long latent period, and effective and cost-effective treatments for diabetes are available. However, three challenges still remain: *1*) a reliable, high-performance, convenient, low-cost screening test that can be universally applied has been lacking; *2*) direct evidence of the benefits and costs of screening are hard to obtain; and *3*) the capacity of health systems worldwide, especially in LMICs, to carry out identification and then to manage the potentially huge new burden of newly identified cases is a concern.

The challenge of a reliable, convenient, low-cost test that may be used widely, especially in LMICs, is potentially soluble. Ritchie el al. (8), for example, present data in this month's issue of *Diabetes Care* indicating that a point-of-care (POC) blood test could be a simple and reliable tool for identifying undiagnosed diabetes. In a population-based study in resource-poor rural South India, Ritchie el al. (8) evaluated a finger-prick fasting capillary POC against fasting venous plasma glucose by systematically screening a random sample of 1,085 participants aged 30 years and older, representing a population of 75,089 from 20 villages. Diabetes was defined according to the 1999 World Health Organization (WHO) criteria of fasting venous plasma glucose of ≥126 mg/dl. They found that the POC fasting capillary test that they used had an area under the curve of 0.87 for detecting diabetes and was significantly better than risk scoring tools that use common clinical variables (age, BMI, hypertension, waist circumference, area under the curve of 0.69). Furthermore, adding clinical variables to their POC fasting capillary test did not significantly improve the discriminatory capability beyond that achieved with the POC glucose alone.

An oral glucose tolerance test or fasting plasma glucose are cumbersome and inconvenient, and the A1C test is expensive and poses special problems with standardization and performance. All of these tests are complex and require skilled health care workers and laboratory facilities for the analysis of samples, which are often a challenge in resource-poor settings. While there have been numerous attempts to develop simple paper and pencil tests to screen for diabetes, these have remained suboptimal, and their performance varies widely by population (9). Therefore, as suggested by WHO, a simple and reliable POC capillary glucose test offers major advantages, but its cost and cost-effectiveness are yet to be ascertained (10).

These results from Ritchie et al. add to the literature on POC capillary glucose tests in resource-poor settings (11,12). While data from Ritchie et al. (8) indicate a realistic potential to develop reliable and convenient low-cost POC tests to detect diabetes, three issues remain to be resolved. Firstly, the performance of capillary POC tests may differ by population characteristics or disease prevalence. For example, POC glucose performed well for detecting diabetes in an Australian indigenous population, but was less discriminatory in a study among Maori (11,12). Further investigations into evaluating a variety of cut points for capillary POC tests in diverse populations may help. Secondly, the costs of POC tests for mass application in LMICs remain a major concern. Ritchie et al. indicate that the POC capillary test, at less than $2 (U.S.) per test, may be inexpensive, but the cost of these tests may need to be many-fold lower before they can be considered for broader use in LMICs. Partnerships with manufacturers in developing countries may help to lower the costs as has been done with cervical cancer tests and with vaccines (13,14). Thirdly, how a POC blood test may be combined with cheaper paper and pencil risk scores remains to be fully explored. While Ritchie et al. (8) point out that their POC capillary test is better than India-specific risk scores, the latter are only a first step to improve the cost-effectiveness of the identification of undiagnosed diabetes.

Given the ethical and logistical challenges of conducting a randomized controlled trial comparing a screening policy versus control, direct evidence for the benefits and costs of screening for diabetes is unlikely to be produced. Recently, however, a number of studies indicate that a policy of early identification of type 2 diabetes may be worth seriously considering. The Anglo-Danish-Dutch study of Intensive Treatment In peOple with screeN-detected diabetes in primary care (ADDITION) trial, whose results were recently reported at an international conference (15), found that primary-care stepwise screening for type 2 diabetes is feasible in settings with good infrastructure and can identify people with

substantial levels of cardiovascular risk. Furthermore, treatment in people with screen-detected diabetes is also feasible, and even in a group that received only routine care, cardiovascular risk factors improved in the 5 years following detection screening. The screen-detected patients who received intensive treatment, however, had greater improvements in prescribed treatment, in levels of risk factors, and also a 12% reduction in cardiovascular death, a 30% reduction in nonfatal myocardial infarction, and a 21% decrease in revascularization, but a nonsignificant 17% reduction in the incidence of a composite cardiovascular primary end point over 5 years. Earlier reports from the ADDITION trial have also indicated that screening for type 2 diabetes is unlikely to be associated with adverse consequences such as anxiety or false reassurance (16). The ADDITION trial was, however, conducted in three countries with established and elaborate nationalized health systems; therefore, translation of these findings into LMICs will remain a challenge that requires a combination of evidence, resources, and socio-political will.

In a simulation model using person-specific data from a representative sample of the U.S. population, Kahn et al. (17) compared eight different screening strategies for type 2 diabetes with a no-screening control strategy. Compared with no screening, all simulated screening strategies reduced the incidence of myocardial infarction (3–9 events prevented per 1,000 people screened) and diabetes-related microvascular complications (3–9 events prevented per 1,000 people screened), and increased the number of quality-adjusted life-years (93–194 undiscounted quality-adjusted life-years) added over 50 years. Screening for type 2 diabetes was found to be especially cost-effective when started between 30 and 45 years of age, with screening repeated every 3–5 years (17). An earlier simulation study, using the Centers for Disease Control and Prevention–Research Triangle Institute (CDC–RTI) diabetes model, had also found opportunistic screening to be within the range of cost-effectiveness when applied to younger populations and minority groups in the U.S. (18).

An additional consideration when thinking about screening for type 2 diabetes is the possibility of coupling it with early identification of nondiabetic dysglycemia, and there are arguments for such an approach. The evidence for the effectiveness and cost-effectiveness of intensive lifestyle intervention or metformin among people with dysglycemia is very strong (19,20). Research also shows that nurses or university graduates can be trained in LMICs to deliver simple and effective preventive health messages to people with dysglycemia and at risk of diabetes (21). Implementation of primary prevention will, however, require an active approach to the identification of dysglycemia, which will also identify undiagnosed diabetes. The recently published results from the Look AHEAD (Action for Health in Diabetes) trial indicates that intensive lifestyle intervention can produce sustained weight loss and improvements in fitness, glycemic control, and cardiovascular disease risk factors in people with type 2 diabetes (22). Identification of dysglycemia and early diagnosis of diabetes, along with intensive treatment with lifestyle intervention for both these groups, can be viewed as inseparable in practice.

Other compelling arguments for an early identification of dysglycemia and diabetes in some populations include the level of risk, the age of onset of diabetes, and the progression rate from dysglycemia to diabetes. For example, people of Asian origin (living in Asia or not) appear to be at high risk of diabetes, develop the disease at younger ages, and rapidly progress from dysglycemia to diabetes (23). In the India Diabetes Prevention Project, 58% of people with impaired glucose tolerance progressed to diabetes within 3 years (24), and even among people with a fasting glucose 100–125 mg/dl (impaired fasting glucose) in Chennai, India, 9% convert to diabetes annually (V.M. Mohan, personal communication). Implementing a policy of screening for both dysglycemia and diabetes may be potentially cost-saving or cost-neutral; within a 3-year horizon and in a health system perspective, screening and preventive management for dysglycemia and diabetes together was found to be cost-saving, relative to no screening, in one regional study (25).

There may be strong reasons to seriously consider active identification and early treatment of dysglycemia and diabetes, especially for specific population groups at very high risk (e.g., Asians, younger people, other ethnic groups at high risk) to potentially avoid the intractable complications that coincide with the subsequent stages of diabetes. Before a policy of active identification can be implemented, however, it is important to carefully weigh the opportunity costs and system capacity. Currently, even those known to have diabetes receive suboptimal care in general, and an active identification policy will add considerable pressures on the system by adding a large number of hitherto undiagnosed cases and also bringing substantial numbers with dysglycemia to the attention of the system. Health care systems, in general, will not have the capacity to deal with the additional workload and the necessity to deliver the appropriate treatment of newly diagnosed diabetes and dysglycemia that will arise with increased testing. Very few systems currently have the orientation and resources to deliver appropriate lifestyle or other preventive interventions.

Regardless of the improvements in the availability of low-cost, convenient tests, such as POC capillary glucose tests or the increasing evidence favoring the benefits of screening for type 2 diabetes, any policy to implement active identification of diabetes/dysglycemia should not be viewed lightly. It will be a huge undertaking and a daunting task for most health care systems, and, if done badly, could cause more harm than good. Despite overwhelming evidence for the prevention of type 2 diabetes, even rich developed countries such as the U.S. are grappling with how to integrate identification of high risk with lifestyle intervention into a large, fragmented curative-focused expensive health care system in which delivery of uniform high-quality care to all people with diagnosed diabetes also remains a challenge. Some recent progress has been made in the U.S. by innovatively merging incentives (e.g., getting health insurance plans to reimburse lifestyle interventions) with community resources (e.g., use of community partners like the YMCA) (26) and also in Finland (27) to advance the prevention of type 2 diabetes and its complications.

At the same time, as the transitioning economies of LMICs like India and China continue to grow rapidly, they both experience the growing burden of diabetes and will likely invest in health and health care. This may be a green-field opportunity to use a policy of active identification of diabetes and dysglycemia as a means to propel health care toward an innovative preventive orientation for noncommunicable diseases (NCDs). For example, primary prevention for type 2 diabetes could serve as the entry point for broader NCD prevention, as most chronic diseases share the same risk factors (i.e., physical activity, healthy nutrition, smoking cessation) (28). Wise experimentation with,

and evaluation of, innovative and integrated prevention-oriented low-cost health care models may allow rapidly transitioning LMICs to leapfrog the long-established developed countries in terms of realigning their systems at a nascent stage and also help avoid and forestall large health and economic burdens due to diabetes and other NCDs. Any strategy for early identification of type 2 diabetes and dysglycemia should be within the context of policy to strengthen and reorient health systems, but the time for action in economically fast growing LMICs is now.

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