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Treatment urgency: The importance of getting people with type 2 diabetes to target promptly

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ABSTRACT

The burgeoning population of individuals with type 2 diabetes provides challenges for management in terms of risk of diabetes-related complications. Early, intensive glycemic control particularly in newly-diagnosed people with type 2 diabetes has been shown to be beneficial in terms of reducing diabetic complications, indeed various national and international guidelines now routinely recommend intensive blood glucose control as an essential element of type 2 diabetes management. However, despite this, current management of glycemia is suboptimal and not enough people achieve their glucose targets worldwide. The Global Partnership for Effective Diabetes Management believe that an improved understanding of these contributing factors should enable the development of practice and guidance that will promote a drive toward better quality clinical outcomes.

Diabetes, and in particular type 2 diabetes (T2DM), is a global epidemic [1]. Estimates from the International Diabetes Federation (IDF) suggested that in 2013 almost 400 million people worldwide had diabetes (which could reach ~642 million by 2040) and, of great concern, approximately half of those people were not aware of their condition [1]. We know that diabetes accounts for 5 million deaths per year, which amounts to >8% of all deaths globally – in fact, every 6 s a person dies from diabetes [1]. In economic terms a staggering US $548 billion was spent on diabetes management in 2013 [1]. What causes more unease is the knowledge that the prevalence and incidence of T2DM are increasing, particularly in non-western countries, in conjunction with higher obesity rates and the 'westernization' of lifestyle [1,2]. T2DM is not the sole preserve of the middle aged or elderly, and it is commonly recognized that the incidence and prevalence of T2DM in youth is rising rapidly in parallel with childhood obesity [3]. Individuals who develop T2DM in their youth are exposed to prolonged hyperglycemia and have a raised risk of early mortality or diabetes complications [3–5], alongside effects beyond the physical and personal that also impact family members and communities.

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The growing diabetes population poses particular challenges for management in terms of comorbidities and established complications of diabetes [6]. The macro- and microvascular complications associated with T2DM are well-known to have a significant detrimental effect on an individual's quality of life. People with T2DM are 2–6 times more likely to develop cardiovascular disease than individuals without diabetes [1] and diabetes is the leading cause of end-stage renal disease, accounting for 50% of all cases in the developed world [7]. Diabetic retinopathy is also a major complication of diabetes (in particular in people with T2DM), and in these individuals their vision may be threatened by diabetic macular edema and proliferative diabetic retinopathy [8]. In developed countries these two conditions are the principal cause of blindness in adults of working age [9]. As well as the aforementioned diseases, T2DM is also associated with an increased risk of neuropathy, amputations, hospitalizations, cancer, serious psychiatric illness, cognitive decline, chronic liver disease, accelerated arthritis, and other disabling conditions [10].

A fundamental component of T2DM control is management of hyperglycemia, with data from the United Kingdom Prospective Diabetes Study (UKPDS) published almost 30 years ago establishing that early, intensive glycemic control in newly diagnosed patients with T2DM significantly decreases rates of microvascular complications (retinopathy, neuropathy and nephropathy) [11]. Moreover, analyses of long-term UKPDS data also showed that patients treated intensively to achieve glycemic control additionally received beneficial effects in terms of cardiovascular disease and total mortality reduction [12]. More recently, an almost 10-year follow up of the Veterans' Administration Diabetes Trial [VADT] [13] found a significant reduction in risk of major cardiovascular events in those assigned to intensive treatment (although no change in total mortality was observed) [14]. Findings from UKPDS and VADT in conjunction with data from other large-scale diabetes studies (such as Action to Control Cardiovascular Risk in Diabetes [ACCORD] and Action in Diabetes and Vascular Disease: Preterax and Diamicron Magnetic Resonance Controlled Evaluation [ADVANCE] [15,16] led to various national and international guidelines now routinely recommending intensive blood glucose control as an essential element of T2DM management [10,17–19] when this can be achieved safely and is appropriate for that individual.

Although the benefits of intensive and early glycemic control are well-documented [20,21], current management of glycemia is suboptimal and not enough people achieve their glucose targets [22]. In fact, as few as 25% of patients achieve their blood glucose goals in some T2DM populations [23] while an analysis from the USA showed that 35% of individuals were not reaching personalized goals [24]. Even in the controlled environment of clinical studies optimal management of glycemia is not always achieved [25,26]. For example, in a prospective study examining treatment intensification programs in T2DM individuals not achieving HbA_{1c} targets, only marginal improvements were observed in the percentage reaching goal after 12 months of more intensive therapy [25] (perhaps highlighting that treatment regimens were not intensive enough). In addition, a study of T2DM patients (n = >17,000) treated with oral antihyperglycemic agents reported that more than 3000 were not at glycemic target and required treatment intensification. However, treatment was intensified (from mono-, combination or triple therapy) in only 39% of those requiring it and a significant delay occurred between the need for action and the change to therapy being initiated – the majority (~60%) of treatment changes were delayed by ⩾6 months and ~40% by more than 1 year [26].

As a consequence of suboptimal glycemic management and delays in treatment intensification or modification, the complications of T2DM resulting from chronic hyperglycemia continue to cause substantial morbidity and mortality [22,27]. Clearly, intensive blood glucose lowering therapy should be employed to reach and maintain the most appropriate HbA1c value in each individual while always considering safety. The question that then arises is what are the factors leading to suboptimal control or failure to intensify therapy, and how can we address them? The *Global Partnership for Effective Diabetes Management*, a multidisciplinary group from leading institutions and diabetes organizations worldwide, has previously developed and refined 10 key recommendations to assist healthcare professionals in ensuring patients achieve and maintain their glycemic targets [17,20,28]. These '*10 steps to get more type 2 diabetes patients to goal*' [28] (Table 1) are a vital part of a patient-centered approach that aims to individualize therapy in terms of glycemic targets and choice of treatment [17]. The *Global Partnership* has become increasingly aware and concerned that outcomes for those with T2DM,

Table 1 – Ten steps to get more type 2 diabetes patients to goal [17].

1. Aim for an appropriate individualized glycemic target, for example, HbA_{1c} 6.5–7% (48–53 mmol/mol) (fasting/preprandial plasma glucose 110–130 mg/dL [6.0–7.2 mmol/L] where assessment of HbA_{1c} is not possible) when safe and appropriate
2. Monitor HbA_{1c} every 3 months in addition to appropriate glucose self-monitoring
3. Appropriately manage all cardiovascular risk factors
4. Refer all newly diagnosed patients to a unit specializing in diabetes care where possible
5. Address the underlying pathophysiology of diabetes, including the treatment of β-cell dysfunction and insulin resistance
6. Treat to achieve appropriate target HbA_{1c} within 6 months of diagnosis
7. After 3 months, if patients are not at the desired target HbA_{1c}, consider combination therapy
8. Consider initiating combination therapy or insulin for patients with HbA_{1c} ⩾ 9% (⩾75 mmol/mol)
9. Use combinations of anti-hyperglycemic agents with complementary mechanisms of action
10. Implement a multidisciplinary team approach that encourages patient self-management, education and self-care, with shared responsibilities to achieve goals