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Should seven be the magic number of type 2 diabetes?

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Abbreviations ADA: American Diabetes Association · ACE: American Association of Clinical Endocrinologists

Seven deadly sins in Dante's purgatory; the seven wonders of the world; and G7, the annual summit that brings together the leaders of the seven wealthiest countries in the world. Is the number seven of similar importance in diabetology? The answer could be yes! In 1997, the Expert Committee of the American Diabetes Association (ADA) [1] revised the criteria for the diagnosis of diabetes to recommend that people with fasting plasma glucose ≥ 7 mmol/l should be classified as suffering from the disease. For a number of years, 7% has been the ADA HbA_{1c} threshold value for satisfactory glycaemic control [2]. However, the most recent recommendations published by the ADA [2] and the American Association of Clinical Endocrinologists (ACE) [3] state that, although HbA_{1c} remains the gold standard for assessing glycaemic control, it is important to consider both fasting and postprandial glucose to achieve HbA_{1c} targets, since HbA_{1c} is determined by fasting and postprandial glucose excursions over a 3-month period. From a mathematical point of view, the theory can be formulated as follows [4]:

$$[\text{HbA}_{1c}]_0^{3\text{months}} = \int_0^3 \text{months FPG}(t) dt + \int_0^3 \text{months PPG}(t) dt$$

where FPG(*t*) and PPG(*t*) are the time courses of fasting and postprandial glucose, respectively.

Such clear concepts should lead to simple recommendations; however, there appears to be a lack of consistency between organisations.

Despite efforts to reach a consensus, discrepancies remain not only between guidelines around the world [5], but also within the same country [2, 3]. The ADA targets are 5.0–7.2 mmol/l (90–130 mg/dl) for preprandial capillary glucose and 10 mmol/l (<180 mg/dl) for peak postprandial capillary glucose, while the ACE targets are more stringent: 6.1 mmol/l (<110 mg/dl) for fasting or preprandial glucose and 7.8 mmol/l (<140 mg/dl) for 2-h postprandial glucose values. These recommendations should be simplified to values that can easily be used by medical practitioners. By using the mathematical enchantment of numbers and, more prosaically, by analysing 480 glycaemic profiles of type 2 diabetic patients not receiving insulin [6], the first two number sevens, defined above, can be joined by additional sevens to complete the series.

A threshold plasma glucose level of 7 mmol/l at 17.00 h (i.e. 5 h after lunch) is optimal for predicting whether HbA_{1c} is less than 7%, as this is associated with the best balance between high sensitivity and specificity (Fig. 1). Furthermore, a value of 7 mmol/l, measured at 14:00 hours, i.e. 2 h after lunch, is the optimal threshold value for predicting treatment success as defined by high-specificity ($\geq 90\%$) HbA_{1c} levels of $<7\%$ (Fig. 1). These data suggest that plasma glucose levels of >7 mmol/l for extended periods after lunch can be considered an interventional threshold for pharmacological treatments. Regular observations of plasma glucose >7 mmol/l at such time points during the day should warn physicians to either initiate new therapeutic strategies or to reinforce ongoing treatments. Furthermore, our data indicate that glucose values <7 mmol/l within 2 h after lunch should be considered as targets for either dietary and/or pharmacological treatments, since such values correspond to HbA_{1c} $<7\%$, with very high specificity, i.e. with a high probability of treatment success.

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Fig. 1 Optimal plasma glucose threshold values for predicting HbA_{1c} of less than 7%. The pharmacological interventional glycaemic thresholds (left arrow) represent the optimal balance between high sensitivity and high specificity (i.e. 7 mmol/l at 17.00 h, 5 h after lunch). The dietary and/or pharmacological glycaemic targets (right arrow) correspond to specificities $\geq 90\%$ (i.e. 7 mmol/l at 14:00 hours). Adapted, with permission, from ref. [6]

In summary, it is suggested that the number seven might be used to indicate a cluster of measures, including diagnosis (≥ 7 mmol/l glucose at fasting), interventional thresholds for completing treatments (≥ 7 mmol/l glucose at 5 h after lunch), targets for achieving treatment success (< 7 mmol/l glucose at 2 h after lunch) and HbA_{1c} goals ($< 7\%$). Indeed, it would be easier for health care providers to memorise a single number than trying to struggle with the current jumble of recommendations and values.

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