Dichotomising the risk of hyperglycaemia into diabetes and prediabetes may render a disservice to patient care

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ABSTRACT

Cardiovascular diseases (CVDs) are the leading cause of death worldwide, accounting for one-third of global mortality. Prediabetes increases the risk of CVDs as well as several other conditions, yet people with prediabetes may not seek intervention, thinking that they do not have diabetes, as the risk of progression may have not been emphasised by the healthcare professional. Accumulating evidence indicates that hyperglycaemia represents a continuum of CVD risk and dichotomising the risk into type 2 diabetes and prediabetes may deter early clinical intervention. It is proffered that the term 'prediabetes' is a misnomer that may disguise a serious condition, fostering complacency and undermining its prognostic significance.

KEYWORDS: prediabetes, cardiovascular disease, risk factor, prognosis, clinical practice

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Cardiovascular diseases (CVDs) are the leading cause of death worldwide, accounting for one-third of global mortality with an estimated death toll of 17.9 million people per annum.[1] One-third of these deaths occur prematurely in people under 70 years of age, with major modifiable risk factors including unhealthy diet, inadequate physical activity, smoking, and drinking.[1] These behaviours may result in hypertension, dyslipidaemia, hyperglycaemia and central adiposity. These modifiable risk factors are often measured in primary care facilities and serve as means to assess the risk of CVDs. During this screening process, people with elevated blood glucose levels (BGLs) are classified to have 'prediabetes' if their BGLs are 140–199 mg/dL (7.8–11.0 mmol/L) or 'diabetes' if their BGLs are 200 mg/dL (11.1 mmol/L) or higher.[2]

It should be noted that the definitions of diabetes and prediabetes based on BGLs are arbitrary, with accumulating evidence suggesting that hyperglycaemia is a metabolic derangement in a continuum. The dichotomy of diabetes and prediabetes does not accurately reflect the risk and may downplay the need for prompt clinical intervention and changes to behaviour. Studies have indicated the increased risk of developing CVDs and heart conditions in people with prediabetes.[3] Chronic hyperglycaemia in people with prediabetes is associated with subclinical myocardial damage and is likely to underpin the protectiveness of sodium–glucose cotransporter (SGLT-2) inhibitors such as dapagliflozin and empagliflozin in mitigating risks of heart failure, even among people without diabetes.[3,4] A 2020 meta-analysis synthesising 129 studies involving a total of more than 10 million participants reported an association between prediabetes and CVD (odds ratio: 1.15; 95% confidence interval (CI): 1.11–1.18).[5] In people with atherosclerotic CVD, this association was even higher at 1.37 (95% CI: 1.23–1.53). When compared with normoglycaemia, the absolute risk difference in prediabetes for CVD was 8.75 (95% CI: 6.41–10.49) per 10,000 person-years in the general population, and 189.77 (95% CI: 117.97–271.84) per 10,000 person-years in people with atherosclerotic CVD.[5] In addition to increasing CVD risk, prediabetes increases the risk of all-cause mortality (odds ratio: 1.13; 95% CI: 1.10–1.17).[5] Moreover, prediabetes is significantly associated with adverse outcomes of other conditions, such as coronavirus disease 2019 (COVID-19) as recently reported by a meta-analysis including more than 3,000 people (odds ratio: 2.58; 95% CI: 1.46–4.56),[6] and increased risk of developing dementia (450 participants, odds ratio: 1.18; 95% CI: 1.04–1.33).[7]

In Australia, prediabetes affects nearly one in six adults.[8] Organisations such as Diabetes Australia advise that while people with prediabetes have a higher risk of developing CVDs, they are not necessarily engaged with healthcare services.[9] People in the community and healthcare providers in Australia, such as GPs, endocrinologists, cardiologists and dietitians, have highlighted the missed opportunities for early intervention to prevent diabetes disease progression.[10] Type 2 diabetes is characterised by a progressive nature that renders it more challenging and costly to manage at more advanced stages, including the requirement for use of polypharmacy and increased rates of hospitalisation. Prediabetes represents a window of opportunity for intervention where prevention of progression to type 2 diabetes may be possible. Early intervention in people without diabetes with elevated BGLs significantly reduces the odds of progression to type 2 diabetes. There is a clear role for early lifestyle intervention that displays greater effectiveness over pharmacological agents such as metformin. However, most people with prediabetes do not seek

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intervention.[9,10] This lack of urgency from people with elevated BGLs may result partly due to the misnomer 'prediabetes', which nulls the person's motivation for the requisite intervention, thinking that they do not have diabetes. It is acknowledged by the International Diabetes Federation that not all people with 'prediabetes' will develop diabetes, further supporting that this term does not accurately reflect the condition.

Other names that have been used to describe the condition, such as 'intermediate hyperglycaemia' and 'non-diabetic hyperglycaemia', inherit the same limitations, conveying lack of insight into the pathophysiology of metabolic conditions that exert prognostic effects in continuum. This may contribute to complacency and adversely influence people's participation in health-promoting behaviours. An international consensus on a term that describes the condition appropriately to prompt action is warranted, considering that the global prevalence of prediabetes is growing rapidly. It is estimated that within a decade, half a billion people worldwide will develop this condition and 70% of them will eventually be diagnosed with diabetes. Large meta-analyses have demonstrated that hyperglycaemia in the prediabetes range is not benign, and it is a risk both for communicable and non-communicable diseases. It is therefore suggested that the misnomer 'prediabetes' should be replaced by a more appropriate term that adequately reflects and clearly communicates the risk to people. The new term must alert the community about the reasons for taking decisive action to prevent disease progression to diabetes and highlight health improvements. Considering that the term 'high blood pressure' has been useful in clinical practice for communicating the message to people more clearly than the term 'hypertension', we proffer that clinicians adopt the term 'high blood sugar' instead of 'prediabetes', to appropriately communicate the real risk to people. Terms such as 'high blood sugar' and 'high blood pressure' are without judgement. They are statements of facts. Starting to use these terms may facilitate reducing the blame. Finally, to improve the chances of a successful outcome, it is paramount to include the community in such discussions to gain an insight regarding what terminology would best resonate. ■

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