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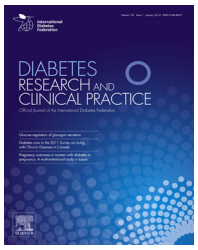

Review

Risk assessment tools for detecting those with pre-diabetes: A systematic review

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ABSTRACT

Aim: To describe and evaluate risk assessment tools which detect those with pre-diabetes defined as either impaired glucose tolerance or impaired fasting glucose using an OGTT or as a raised HbA1c.

Methods: Tools were identified through a systematic search of PubMed and EMBASE for articles which developed a risk tool to detect those with pre-diabetes. Data were extracted using a standardised data extraction form.

Results: Eighteen tools met the inclusion criteria. Eleven tools were derived using logistic regression, six using decision trees and one using support vector machine methodology. Age, body mass index, family history of diabetes and hypertension were the most frequently included variables. The size of the datasets used and the number of events per variable considered were acceptable in all the tools. Missing data were not discussed for 8 (44%) of the tools, 10 (91%) of the logistic tools categorised continuous variables, external validation was carried out for only 7 (39%) of the tools and only 3 tools reported calibration levels.

Conclusions: Several risk scores are available to identify those with pre-diabetes. Before these are used in practice, the level of calibration and validity of the tools in the population of interest should be assessed.

Contents

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Abbreviations: T2DM, type 2 diabetes mellitus; IGR, impaired glucose regulation; IGT, impaired glucose tolerance; IFG, impaired fasting glucose; AUROC, area under the receiver operator curve; ADA, American Diabetes Association; EPV, events per variable.

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1. Background

The prevalence of Type 2 diabetes Mellitus (T2DM) is predicted to steeply rise globally over the next few decades, from the currently estimated 382 million to 592 million by 2035 [1]. This is of particular concern as T2DM can remain undetected, and therefore untreated, for many years. There are numerous long-term complications linked to T2DM including heart disease, blindness and kidney disease [2]. Furthermore T2DM can reduce an individual's life expectancy by as much as 10 years [3].

Impaired Glucose Regulation (IGR) is a pre-diabetic state where either Impaired Glucose Tolerance (IGT) and/or Impaired Fasting Glucose (IFG) have been identified [4]. It has been shown that those with IGR are significantly more likely to develop T2DM than those with normal blood glucose levels; estimates of progression to T2DM within a year suggest those with isolated IGT have over five times the risk, those with isolated IFG have seven times the risk and those with both IGT and IFG have over 12 times the risk compared to normoglycemic individuals [5]. There are now also recommendations that HbA1c levels raised above normal levels, but not elevated enough for a diagnosis of T2DM, should be classified as at high risk of diabetes [6,7]. However there is no agreed consensus on the HbA1c range that should be classified as at high risk of diabetes, with the International Expert Committee and the UK-based National Institute for Health and Clinical Excellence recommending it be 6.0–6.4% (42–46 mmol/mol) whereas the American Diabetes Association (ADA) suggests 5.7–6.4% (39–46 mmol/mol) [7–9]. Follow-up studies have shown similar rates of progression to diabetes from the HbA1c defined pre-diabetic state as seen for IFG [10]. Throughout this study we term the composite of IGT and/or IFG or elevated HbA1c according to any recommended definition [7–9] as pre-diabetes.

Lifestyle and pharmacological interventions have been shown to delay or even prevent T2DM in those with pre-diabetes [11–14]. Thus one approach to tackling the increasing prevalence of T2DM is to identify those with pre-diabetes and offer such intervention. Risk assessment tools can be developed to predict the probability of a particular health outcome for an individual given their characteristics (risk factors). Risk assessment tools help to optimise resources required for detecting diseases, which are often limited, by allowing screening to be targeted at those with the highest risk [15]. Thus in order to identify those with pre-diabetes, whom may benefit from intervention, risk assessment tools are valuable, with many advocating them as the first stage in a screening programme [7].

Several systematic reviews of risk tools for T2DM outcomes (either current undiagnosed T2DM or incident of T2DM (or both)) have recently been published [16–21]. These reviews found that while the predictive performances of the available tools were moderate to high on internal data, they performed poorly on external data; raising concerns about methodology used to develop the scores and their ability to discriminate between those with and without the condition when used in practice. To date no systematic reviews have focussed on detecting those with pre-diabetes. This review aims to identity and summarise tools developed which detect those with pre-diabetes. The methodological quality of the tools identified will also be evaluated.

2. Methods

2.1. Search strategy

All articles which developed new risk assessment tools for undiagnosed pre-diabetes with or without undiagnosed T2DM were identified. The following electronic sources were searched: Medline (1946 until 7th January 2013); Embase (1974 until 7th January 2013). Databases were searched using a specific search strategy, given in Appendix A. Reference lists of relevant articles were also manually searched. Grey literature, understood as unpublished or un-indexed work, was included in this review; however conference abstracts were not considered as the full article was required.

2.2. Inclusion/exclusion criteria

The outcome of a risk assessment tool for inclusion had to be one of the following:

1. IGR (IFG and/or IGT using OGTT) [4]
2. Pre-diabetes by HbA1c using any recommend definition [7–9]
3. 1 and 2
4. 1 or/and 2 and current undiagnosed T2DM (by HbA1c or using OGTT).

The risk assessment tools had to contain two or more risk factors. Articles only assessing associations were excluded. Risk tools that included genetic factors were excluded as they are often expensive and time-consuming to collect so do not offer the same benefits over diagnostic tests that other non-genetic risk tools do. The risk tools had to be developed either on a population-based sample or volunteers/opportunist sample, i.e. not a pre-screened sample, for example individuals at an obesity clinic. In order for the methodology to be assessed the article had to detail the development of the risk tool. Finally this review was restricted to articles published in English.

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