Summary

Diabetes is the fastest growing chronic disease worldwide. Conventional diagnostic tests, such as fasting plasma glucose, oral glucose tolerance test and glycosylated hemoglobin, are invasive and relatively expensive for application in low-income developing countries. Diabetes Risk Score has emerged as a practical screening tool during the past decade. The purpose of this review is to evaluate the components and validity of risk scores for the screening and early detection of Type 2 diabetes mellitus.

Practice Points

- Although conventional diagnostic tests for Type 2 diabetes mellitus screening are reliable, they are invasive and relatively expensive.
- Diabetes Risk Score (DRS) has been developed and implemented in various countries during the past decade.
- Components of the published risk scores ranged from three items for the northern Chinese risk score, to ten items for the German risk scores.
- These items or questions were derived from primary studies where risk factors or components were generated.
- The validity of the DRS appears to vary between countries, with sensitivity and specificity ranging from 69.0 to 84.2%, and 39.8 to 76%, respectively.
- The main components found in these risk scores are age, waist circumference, hypertension, family history, BMI and physical inactivity.
- The diversity of risk scores is necessary for application to various populations.
- Validity is relatively high despite the different methods used in primary studies to derive such risk scores.
- Since DRS is a simple and inexpensive tool, it will become more popular for the screening and early detection of Type 2 diabetes mellitus, especially in Asian developing countries.
- DRS should be developed and validated based on large-scale population studies using established diagnostic criteria for Type 2 diabetes mellitus before its application.

Despite DRS being a simple and inexpensive tool, it will become more popular for the screening and early detection of Type 2 diabetes mellitus, especially in Asian developing countries.

DRS should be developed and validated based on large-scale population studies using established diagnostic criteria for Type 2 diabetes mellitus before its application.
Type 2 diabetes mellitus (T2DM) is now of pandemic proportions in most continents and shows no signs of abatement [1–3]. It affects 246 million people worldwide, and this is projected to rise to 380 million by 2025, according to the International Diabetes Federation [101]. From a public health perspective, primary prevention would be the most effective way to combat the rising trend, and to reduce the disease burden in terms of mortality, morbidity and costs to the healthcare system and to society.

Several conventional diagnostic tests have been recommended for T2DM screening by WHO, including fasting plasma glucose, oral glucose tolerance test and glycosylated hemoglobin [102]. Although these tests are reliable, they are invasive and relatively expensive [4]. Furthermore, their application for screening in low-income countries is less feasible because of cost and other constraints, including the lack of qualified technicians and equipment [5]. A simple, effective and noninvasive assessment tool could be useful in screening for those with, or who have the potential to develop, T2DM in developing countries. Since the introduction of the Diabetes Risk Score (DRS) in Finland, the method has been continually developed and implemented in various countries during the past decade. Nevertheless, the components and validity of these DRSs have not been extensively assessed in the literature. The purpose of this review is to evaluate the components and validity of DRS, with particular attention given to those DRSs developed for population screening of T2DM in general and not the prediction of risk for individuals.

Method

To search for available DRSs during the period 2000–2011, a combination of the keywords ‘risk score’, ‘diabetes risk score’, ‘Type 2 diabetes’, ‘diabetes’, ‘screening tool’ and ‘diagnostic test’ were used. The following online databases were searched for articles published in the English language: Pubmed, Science Direct, Web of Knowledge and Google Scholar. However, published reviews, commentary and books that did not provide primary data on the validation of DRS were excluded. After retrieving the full text of relevant articles, their reference lists were manually checked to identify additional articles missing from the main electronic search. Duplicate reports in which data were published elsewhere were subsequently removed from further consideration. Finally, all full-text articles on risk scores that do not rely on biological or invasive measures were reviewed. The search was conducted by a single investigator (first author) at the end of 2011.

Essential information concerning the use of the DRS was extracted from each article and summarized. This included primary study design (models to generate risk factors or components of DRS), population, sample size, age group, DRS cut-off values, sensitivity, specificity, scoring scale and number of questions or components. In addition, the value of the area under receiver operating characteristic (ROC) analysis that produced the optimal cut-off value of each DRS was tabulated.

Results

Initial searches for articles in PubMed using the prescribed keywords returned 4158 citations. Further refinement limiting the search to the English language, publication within the past 10 years and human-related studies resulted in 2856 full-text journal articles. After restricting to those with “diabetes risk score” appearing in the title only, 19 articles met the criteria. The same search procedure was then applied to other databases, which led to 41 articles. In total, 60 articles were found from searching these electronic online databases. Thirty-six articles lacking primary studies to validate DRS were then excluded. Finally, after careful inspection of the content of the retrieved articles and their reference lists manually, ten relevant articles were selected for detailed review.

The primary study designs that generated the DRS were either cohort (7/10) or cross-sectional survey (3/10), using logistic regression analysis to determine significant risk factors for deriving the DRS. The sample sizes of these primary studies ranged from 2350 (India) to 25,167 (Germany), and an adult population aged 17 years and above was used to develop and validate DRS.

Table 1 presents the components or questions of the DRS developed and validated for T2DM screening by country. There are nine countries, namely, the USA [6], Finland [7], Germany [8], Australia [9], India [10], Thailand [11], China (south [12] and north [13]), Oman [14] and Denmark [15], involving 20 components. Besides age, which is used in all ten studies, the most common items are hypertension, waist circumference and family history. Some items are protective factors for T2DM; for example, coffee intake and eating vegetables/fruits; whereas race is an important factor.
Table 1. Components and corresponding scores of published diabetes risk scores in ten studies.

<table>
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<tbody>
<tr>
<td>Age</td>
<td>5</td>
<td>3</td>
<td>4.3</td>
<td>8</td>
<td>30</td>
<td>2</td>
<td>12</td>
<td>12</td>
<td>9</td>
<td>18</td>
</tr>
<tr>
<td>Waist circumference</td>
<td>35</td>
<td>4</td>
<td>7.4</td>
<td>7</td>
<td>20</td>
<td>2</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Hypertension</td>
<td>11</td>
<td>2</td>
<td>46</td>
<td>2</td>
<td>–</td>
<td>2</td>
<td>3</td>
<td>–</td>
<td>3</td>
<td>10</td>
</tr>
<tr>
<td>Family history</td>
<td>21</td>
<td>–</td>
<td>–</td>
<td>3</td>
<td>20</td>
<td>2</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>BMI</td>
<td>–</td>
<td>3</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>5</td>
<td>8</td>
<td>–</td>
<td>3</td>
<td>15</td>
</tr>
<tr>
<td>Physical inactivity</td>
<td>–</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>30</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>6</td>
</tr>
<tr>
<td>Male gender</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>3</td>
<td>–</td>
<td>2</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Smoking</td>
<td>4</td>
<td>–</td>
<td>24/64</td>
<td>2</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Height</td>
<td>8</td>
<td>–</td>
<td>–3.4</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>History of high blood glucose</td>
<td>–</td>
<td>5</td>
<td>6</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Race</td>
<td>6</td>
<td>–</td>
<td>–</td>
<td>2</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Eating vegetables/fruit</td>
<td>–</td>
<td>1</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Whole grain bread</td>
<td>–</td>
<td>–</td>
<td>–9</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Gestational diabetes</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>2</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Weight</td>
<td>5</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
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<tr>
<td>Resting pulse</td>
<td>5</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Dyslipidemia</td>
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<td>–</td>
<td>–</td>
<td>–</td>
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<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
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<tr>
<td>Consumption of red meat</td>
<td>–</td>
<td>49</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Moderate alcohol intake</td>
<td>–</td>
<td>–</td>
<td>–20</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Coffee intake</td>
<td>–</td>
<td>–</td>
<td>–4</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Total score</td>
<td>100</td>
<td>20</td>
<td>–</td>
<td>35</td>
<td>100</td>
<td>17</td>
<td>30</td>
<td>32</td>
<td>25</td>
<td>60</td>
</tr>
<tr>
<td>Low risk for T2DM</td>
<td>&lt;38</td>
<td>&lt;9</td>
<td>&lt;500</td>
<td>≤5</td>
<td>≤60</td>
<td>&lt;6</td>
<td>&lt;8</td>
<td>&lt;14</td>
<td>&lt;10</td>
<td>&lt;31</td>
</tr>
<tr>
<td>High risk for T2DM</td>
<td>≥38</td>
<td>≥9</td>
<td>≥500</td>
<td>≥12</td>
<td>&gt;60</td>
<td>≥6</td>
<td>≥16</td>
<td>≥14</td>
<td>≥10</td>
<td>≥31</td>
</tr>
</tbody>
</table>

¹Coefficients to calculate scores.
†Former smoker/current heavy smoker.
²T2DM: Type 2 diabetes mellitus.

component of DRS for racially diverse countries (USA and Australia). The number of components and the scoring system are found to vary between countries, ranging from three (north China) to ten (Germany) components, and from 17 points (Thailand) to 100 points (India and USA), respectively. Only the DRS from India and Australia were not externally validated.

Table 2 summarizes the characteristics of the DRS systems. Seven of the ten DRS were validated using the WHO diagnostic criteria for T2DM [102]. One study was validated based on the American Diabetes Association guidelines [16], and another study was validated using the diagnostic criteria for T2DM of WHO and the International Diabetes Federation [103]. The study conducted in Germany adopted a diagnostic criteria similar to the WHO test, but with oral glucose being replaced by 75 g dextrose. The ROC values of these DRS also varied between populations (average 0.77). The lowest ROC value was 0.67 in north China, and the highest was 0.87 in Finland. Sensitivity and specificity ranged from 69.0 to 84.2% and 39.8 to 76%, respectively.

Discussion

Components of DRS

The number of components used in developing DRS ranged from three to ten. Although a DRS with fewer questions would be easier to administer, T2DM is known to involve gene–environment interaction with multiple causal factors [17]. Each risk score was developed based on a primary study targeting a particular population at a certain time. Therefore, the number of components...
Table 2. Characteristics of published diabetes risk scores in ten studies.

<table>
<thead>
<tr>
<th></th>
<th>USA</th>
<th>Finland</th>
<th>Germany</th>
<th>Australia</th>
<th>India</th>
<th>Thailand</th>
<th>South China</th>
<th>North China</th>
<th>Oman</th>
<th>Denmark</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of components</td>
<td>9</td>
<td>7</td>
<td>10</td>
<td>9</td>
<td>4</td>
<td>6</td>
<td>6</td>
<td>3</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Scoring system</td>
<td>0–100</td>
<td>0–20</td>
<td>118–983</td>
<td>0–35</td>
<td>0–100</td>
<td>0–17</td>
<td>0–30</td>
<td>3–32</td>
<td>0–25</td>
<td>0–60</td>
</tr>
<tr>
<td>ROC value</td>
<td>0.71</td>
<td>0.87</td>
<td>0.84</td>
<td>0.78</td>
<td>0.69</td>
<td>0.74</td>
<td>0.74</td>
<td>0.67</td>
<td>0.83</td>
<td>0.80</td>
</tr>
<tr>
<td>Criteria for T2DM</td>
<td>WHO</td>
<td>WHO</td>
<td>WHO</td>
<td>WHO</td>
<td>ADA</td>
<td>WHO</td>
<td>WHO/IDF</td>
<td>WHO</td>
<td>WHO</td>
<td>WHO</td>
</tr>
<tr>
<td>Study design</td>
<td>Cohort</td>
<td>Cohort</td>
<td>Cohort</td>
<td>Cohort</td>
<td>Cohort</td>
<td>Cross-sectional</td>
<td>Cross-sectional</td>
<td>Cross-sectional</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sample size</td>
<td>9587</td>
<td>4435</td>
<td>25,167</td>
<td>6060</td>
<td>2350</td>
<td>2677</td>
<td>2448</td>
<td>4336</td>
<td>4881</td>
<td>6784</td>
</tr>
<tr>
<td>Target age group</td>
<td>45–64</td>
<td>45–64</td>
<td>&gt;55</td>
<td>&gt;75</td>
<td>&gt;75</td>
<td>&gt;75</td>
<td>&gt;75</td>
<td>&gt;75</td>
<td>&gt;75</td>
<td></td>
</tr>
<tr>
<td>Sensitivity (%)</td>
<td>69.0</td>
<td>81.0</td>
<td>83.1</td>
<td>74.0</td>
<td>72.5</td>
<td>77.0</td>
<td>84.2</td>
<td>78.6</td>
<td>75.9</td>
<td></td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>64.0</td>
<td>76.0</td>
<td>68.3</td>
<td>67.7</td>
<td>60.1</td>
<td>60.0</td>
<td>39.8</td>
<td>73.4</td>
<td>72.2</td>
<td></td>
</tr>
</tbody>
</table>

ADA: American Diabetes Association; IDF: International Diabetes Federation; ROC: Receiver operating characteristic; T2DM: Type 2 diabetes mellitus.

should be considered carefully and validated for each specific case [18]. Obviously, those DRSs with more components would be time consuming and costly to administer in the community setting. Diversity of scales is also found among the DRS systems, which ranged from 17 to 100 points. Most of them used one cut-off value to classify high risk or low risk of T2DM. However, there are two DRS-adopted cut-offs for separation into low-risk, moderate-risk and high-risk groups [9,12].

In total, 20 components are involved in these ten validated DRSs. The most common risk factors, such as age, waist circumference and hypertension, were produced from reliable prospective studies with large sample sizes [4]. All ten DRSs included age. Aging has been found to be associated with physiological changes in homeostasis, body composition, hormones, free fatty acids and glucose, which may cause impairment of insulin secretion and action [19]. Epidemiological studies have also suggested that elevated prevalence of T2DM significantly associated with the aging population [20].

Eight of the ten reviewed DRSs used hypertension history as an essential question. Hypertension is an important risk factor for T2DM. It is known that the use of β blockers can help control high blood pressure. However, some observations have indicated that a greater number of new-onset diabetes cases were recorded in those administered with β blockers with or without diuretics, when compared with others using calcium channel blockers or angiotensin-converting enzyme [21,22].

A family history of diabetes is another common component of the reviewed DRSs. Associations between genetic factors and both Type 1 and Type 2 diabetes have been demonstrated. Among the 40 loci of diabetic human genes, the TCF7L2 locus is believed to contribute to β-cell dysfunction and lead to T2DM [23]. In addition, epidemiological studies have provided evidence on the familial risk of T2DM [24].

BMI has been used to classify overweight and obese patients, and it is an established risk factor for T2DM [25]. Even though BMI was not included in the American DRS, height and weight were used instead for screening T2DM. Waist circumference is used as an alternative to BMI [26]. Moreover, susceptible people who have a chronic excess energy intake do not just store energy in subcutaneous adipose tissue, but around internal organs such as the heart, liver and gut, called visceral adipose tissue. Therefore, waist circumference seems to provide a better reflection for excessive energy balance in the human body and is closely related to mortality [23,27,28].

Although physical inactivity has been known as a lifestyle risk factor for T2DM, it was excluded from several DRSs [29]. In Thailand, for example, the reason for its exclusion was a lack of data in the cross-sectional study [30]. In north China, sedentary lifestyle (physical inactivity) did not show up as a significant predictor for risk of T2DM in the validation study [13].

Contrary to expectations, smoking was not a common component among the DRS systems. Despite its effect on reducing body weight,
Components & validity of risk scores for screening for Type 2 diabetes mellitus

Review

Smoking is associated with an increase in central adiposity, hyperglycemia and dyslipidemia [31]. Smoking also contributes to an increase in inflammation and oxidative stress and it impairs β-cell function [32]. Smoking has been confirmed to damage insulin sensitivity and glucose tolerance [33]. Therefore, current evidence supports a causal relationship between smoking and T2DM [34]. Nevertheless, smoking did not emerge as a significant predictor and consequently was excluded from the DRS in six countries. A plausible reason may be that some risk scores (Thailand, China and Denmark) simply classified smoking status as a dichotomous variable without full consideration of the amount and duration of cigarette smoking exposure [35].

Validities of DRS

The validity of these DRSs depends on factors such as primary study design, sample size, ROC value, sensitivity and specificity. With regard to study design, some DRSs were derived from population-based cross-sectional studies. The level of evidence was thus less reliable than those based on cohort studies [36,37]. Moreover, some studies did not provide adequate data for generating predictors [38,39]. For example, the Thai DRS could not include smoking and physical inactivity because of a lack of data on these variables [11]. Most of the DRSs validated in developed countries were based on cohort studies, whereas low-income countries with limited financial resources relied on data from population-based survey or cross-sectional studies, which may lead to an over-estimation of risk of T2DM [10,40]. In addition, reclassification ability of the DRS was generally not considered for inclusion of new components, with the exception of the north China DRS, which used the net reclassification index to evaluate its performance.

It is important for a DRS to discriminate people at low risk from those at high risk of T2DM. The ROC curve provides a graphic representation of the trade-off between false-positive rates and true-positive rates [41]. Using ROC to determine the optimal cut-off point has the advantage of producing an accurate separation into dichotomous diagnoses (disease vs non-disease). The ROC curve is an effective method of evaluating the overall performance of diagnostic tests [42]. Among the reviewed DRS, the lowest ROC value was 0.67 in the north China study, which means that the cut-off value for this risk score has a 67% success rate for accurately discriminating true positive results, noting that a ROC value of 0.5 for a diagnostic test implies a pure chance. A possible explanation for the lower ROC values of the DRS in the Asian countries is the use of fewer variables in the Asian DRS compared with those in European countries.

Sensitivity and specificity play a vital role in a screening program [37]. The average sensitivity and specificity are 77.3 and 64.6%, respectively, for the DRS in this review. Epidemiological studies have demonstrated that up to 60% of T2DM cases can be preventable by adopting a healthy diet and lifestyle [43,44]. However, there is often a trade-off between sensitivity and specificity, with increases in one measure along with decreases in the other measure. For example, with approximately 85% sensitivity in the north Chinese score [13], 15% of T2DM patients in the target population would be tested negative and thus lose their chance to be detected earlier and treated. Its specificity of approximately 40% implies that 60% of healthy people would be tested as (false) positive. Although it is a noninvasive diagnostic tool, the psychological effect of referring healthy people as ‘diabetic’ can be problematic. Furthermore, healthcare and familial cost burden would increase after the screening test due to these limitations [37]. Therefore, screening hypertensive individuals or those aged over 55 years was considered more cost effective than universal screening [45].

Conclusion

The main components among the ten reviewed DRSs were age, waist circumference, hypertension, family history, BMI and physical inactivity. According to ROC value, sensitivity and specificity, validity of these DRSs is relatively high despite the different study designs and methods used in primary studies to derive such risk scores. The diversity of the scoring systems is necessary for application to various populations.

Future perspective

Diabetes is the fastest growing chronic disease worldwide and Asia has the largest number of cases [46]. Since DRS is a simple and inexpensive tool, it will become more popular for the screening and early detection of T2DM. Over the coming years, it is expected that new DRS systems will emerge from Asian developing countries. However, such DRSs should be developed based on large-scale primary cohort
studies and validated in the population using the established diagnostic criteria for T2DM prior to their application. It is recommended that standardized guidelines [47,48] be formulated for the development and validation of DRXS, especially for developing countries. Areas for future research include interventions that encourage people to check their diabetes risk themselves, and use of DRS on population data sets to determine high-risk subgroups [39].

Financial & competing interests disclosure
The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

References
Papers of special note have been highlighted as:
• of interest
  • of considerable interest
4. Type 2 diabetes is fast increasing in Asian countries.
9. The first Diabetes Risk Score (DRS) was developed and validated in Finland.
14. Simple risk score developed and validated to optimize the cost of screening.
22. A comparison between DRS and other risk scores in European countries.
26. Simple risk score developed and validated to optimize the cost of screening.
34. A comparison between DRS and other risk scores in European countries.
Components & validity of risk scores for screening for Type 2 diabetes mellitus

Review


- Comprehensive review of existing DRSs and prediction models that show that standardized DRSs depend not only on statistical properties, but also on the context of application.


- Guidelines for application of prediction models in health research study.


- Consecutive steps to evaluate the performance of prediction models when applying to new individuals and populations.

Websites

