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Date

Comparing the performance of FINDRISC, CANRISK, and a Saudi-specific dysglycemia risk score
in the Kingdom of Saudi Arabia

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in the Kingdom of Saudi Arabia

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Abstract

Comparing the performance of FINDRISC, CANRISK, and a Saudi-specific dysglycemia risk score in the Kingdom of Saudi Arabia

By Angela Wenxia Guo

Objective: To assess the performance of three diabetes risk scores: a rapid Saudi-specific dysglycemia risk score, the Finnish Diabetes Risk Score (FINDRISC), and the Canadian Diabetes Risk Assessment (CANRISK) as a screening tool for dysglycemia, using data from the Saudi Household Interview Survey, a recent nationally representative cross-sectional study in Saudi Arabia.

Research Design and Methods: Data from 4,461 Saudi adults aged 15 years or older who participated in the Saudi Health Interview Survey and completed an HbA1c lab test were included in the analysis. Anthropologic measurements, socio-demographic information, lifestyle information, and past medical history were collected through household surveys. Participants were referred to a local clinic to complete biochemical measurements, including HbA1c. We assessed the performance of a Saudi-specific risk score, the FINDRISC, and CANRISK tools by calculating sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). We also estimated the kappa statistic for agreement for each risk score to assess the frequency of the risk scores predicting dysglycemia when true dysglycemia was present, and no dysglycemia when true dysglycemia was not present.

Results: Overall, CANRISK was the most sensitive in identifying those with dysglycemia (CANRISK: 70.57% [70.54, 70.59] vs. Saudi-specific score: 53.58% [51.36, 55.80] vs. FINDRISC: 39.46% [39.43, 39.49]), but the least specific in detecting those without dysglycemia (CANRISK: 55.87% [55.85, 55.89] vs. Saudi-specific score: 75.54 [73.86, 77.21] vs. FINDRISC: 82.95 [82.83, 82.86]). The PPV was similar among the three risk scores, ranging from 55.2%–63.9%. The NPV was also similar among the three risk scores, ranging from 64.0%–71.2%. The Saudi-specific score had the highest kappa statistic (Saudi-specific score: 0.296, se=0.014; CANRISK: 0.260, se=0.015; FINDRISC=0.233, se=0.014) and demonstrated the best balance in correctly detecting individuals with and without dysglycemia. All three risk scores performed better in identifying individuals with diabetes, compared to identifying individuals with dysglycemia. All three risk scores did not perform as well when detecting undiagnosed dysglycemia and undiagnosed diabetes.

Conclusion: Based on our analysis, the rapid Saudi-specific dysglycemia risk score performs as well as the FINDRISC and CANRISK.

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CHAPTER 1: INTRODUCTION

Introduction:

The burden of diabetes is growing globally, in nearly all countries of the world (Shaw, Sicree, & Zimmet, 2010). An estimated 415 million adults worldwide were affected by diabetes mellitus in 2015 (International Diabetes Federation, 2015). Additionally, an estimated 318 million adults were affected by impaired glucose tolerance, a form a prediabetes which is a precursor to diabetes (International Diabetes Federation, 2015). With a projected 642 million adults expected to be affected by diabetes by 2040, finding ways to manage, control, and prevent the disease will be of upmost importance (International Diabetes Federation, 2015).

The Middle East and North Africa (MENA) region has the second highest diabetes prevalence in the world, second only to Polynesia and Micronesia (NCD Risk Factor Collaboration, 2016). According to the International Diabetes Federation Atlas, 35.4 million adults in the MENA region were estimated to be affected by diabetes in 2015, with that number projected to double by 2040 (2015). It appears that increases in diabetes in this region are occurring parallel to economic development, rapid urbanization, and may be related to increasingly sedentary lifestyles, poor diet, and increased life expectancy (Anokute, 1990; Murad, Abdulmageed, Iftikhar, & Sagga, 2014; Sherif & Sumpio, 2015).

Natural History of Type 2 Diabetes Mellitus

The two most common forms of diabetes mellitus are Type I diabetes and Type 2 diabetes. Type 1 diabetes is an autoimmune disorder involving the destruction of beta-cells in

the pancreas and is generally diagnosed during childhood. Since beta-cells of the pancreas produce insulin, individuals with Type 1 diabetes are unable to produce insulin. Treatment for Type 1 diabetes is typically daily insulin injections (Story & Stang, 2005).

Type 2 diabetes is caused by the loss of beta cell function and insulin-resistance. Type 2 diabetes is typically diagnosed during adulthood and is managed with a combination of lifestyle modification, oral medications, and/or insulin (Story & Stang, 2005). For the purposes of this report, I will focus solely on Type 2 diabetes.

The natural history of Type 2 diabetes includes an asymptomatic or subclinical stage, referred to as prediabetes which can be characterized as a state of impaired fasting glucose, impaired glucose tolerance, or both. This stage before the onset of diabetes occurs when blood glucose levels are elevated above normal levels, but have not reached the threshold for a positive diagnosis of diabetes (Tabák, Herder, Rathmann, Brunner, & Kivimäki, 2012). Dysglycemia refers to this subclinical phase and Type 2 diabetes; in other words, any elevation of blood glucose level beyond what is considered normal.

Diabetes is associated with increased mortality from cardiovascular disease, and is a leading cause of blindness, renal failure, and lower limb amputation worldwide. (Susan van, Beulens, Yvonne T. van der, Grobbee, & Nealb, 2010). Complications of the disease can lead to profound social and financial costs. For individuals, the consequences of diabetes can prevent them from being able to work, be socially stigmatizing and debilitating. Diabetes is a costly disease to treat and manage for individuals and health systems as it requires long-term management and care (Alhowaish, 2013; Susan van et al., 2010; Whiting, Guariguata, Weil, & Shaw, 2011).

For these reasons, it is imperative for countries in the Middle East and North Africa (MENA) region to address rising rates of diabetes and identify those at high risk of developing the disease to focus prevention efforts, and to ensure that those with the disease receive the proper treatment to prevent further complications from the disease. Given that an estimated four out of ten adults with diabetes in the MENA region are undiagnosed, identifying these individuals will be a major challenge for countries in that region (International Diabetes Federation, 2015).

Type 2 Diabetes in Saudi Arabia

Type 2 diabetes is a growing health concern for the Kingdom of Saudi Arabia. Numerous studies have been done to measure the prevalence of diabetes in the country. A systematic review of such studies found that diabetes prevalence ranged from 2.5% in 1982 to as high as 31.6% in 2011 (Zabetian, Keli, Echouffo-Tcheugui, Narayan, & Ali, 2013). In order to support data-driven decision-making and to generate less variable estimates regarding diabetes status in Saudi Arabia, the Ministry of Health of Saudi Arabia conducted the Saudi Health Interview Survey (SHIS) in 2012. SHIS is a national cross-sectional survey of individuals aged 15 years or older. SHIS used multistage sampling to recruit a population sample that was considered representative of the country's residents. Preliminary findings from this data suggest that 13.4% of the adult population in Saudi Arabia has diabetes, with more than half of those with diabetes are undiagnosed (El Bcheraoui et al., 2014). The same study also estimated that 15.2% of the adult population had borderline diabetes, and are at high risk for developing diabetes. The proportion of individuals with borderline diabetes that were aware of their condition was

not reported. A study in the United States that found only 11.1% of individuals with borderline diabetes were aware of their status (Centers for Disease Control and Prevention, 2013). This would likely be similar or lower in Saudi Arabia as well. With a large proportion of those with diabetes and borderline diabetes remaining undiagnosed, there is a need to effectively screen for individuals with diabetes and prediabetes in Saudi Arabia (El Bcheraoui et al., 2014).

There are several studies that have examined what specific risk factors in the region predispose the Saudi and MENA populations to diabetes. A study looking at risk factors for cardio-metabolic diseases in the MENA region found that suboptimal diets, in particular low vegetable and fruit intake, and sub-optimal systolic blood pressure were the leading risk factors for cardio-metabolic disease mortality in nearly all of the countries in the region (Afshin et al., 2015). A case control study done in the Al-Qassim region in Saudi Arabia found that there was a strong association between diabetes and maternal history of diabetes, education, lack of exercise, and dietary habits (Midhet, Al-Mohaimeed, & Sharaf, 2010). Another case control study done in Jeddah found that individuals with diabetes were more likely to be men, less educated, natives of eastern Saudi Arabia, retired, lower-salaried, married or divorced, current smokers, hypertensive, obese, and have family history of diabetes (Murad et al., 2014). A study using data from the Saudi Household Interview survey found that 33.5% of Saudi women and 24.5% of Saudi men were obese, and that obesity was strongly associated with diabetes (Memish et al., 2014).

Screening for Type 2 Diabetes

According to the World Health Organization, “screening is the process of identifying those individuals who are at sufficiently high risk of a specific disorder to warrant further investigation or direct action” (World Health Organization, 2003). Screening for Type 2 diabetes can be justified using the Wilson and Jungner criteria for screening which states that, screening should only be done if the disease is an important health problem with available and acceptable treatment, if there are resources for diagnosis and treatment of the disease, and if there is an acceptable test for the early symptomatic or latent stage of the disease (Wilson & Jungner, 1968). Type 2 diabetes meets all these requirements as it is a major health problem that is a leading cause of morbidity globally, there are available diagnostic tests to detect the presence of the disease, including in latent or subclinical phases, and there are available and acceptable treatments for the disease (Echouffo-Tcheugui, Ali, Griffin, & Narayan, 2011; Sheehy, Coursin, & Gabbay, 2009).

Furthermore, there is considerable and robust evidence regarding the efficacy of interventions to prevent complications among people with diabetes, through adherence to healthy lifestyle choices (e.g., avoiding tobacco use) and medications to manage glucose, blood pressure, and cholesterol (Chalmers & Arima, 2009; Cholesterol Treatment Trialists, 2015; Mohiuddin et al., 2007; Nathan et al., 2005; Tandon, Ali, & Narayan, 2012; UK Prospective Diabetes Study (UKPDS) Group, 1998). Early detection of diabetes can lead to better management of the disease and prevent the development of further complications. (Susan van, Beulens, Yvonne T. van der, Grobbee, & Nealb, 2010).

Individuals with borderline or prediabetes have a five to ten times higher annual risk of developing diabetes compared to people with normal glucose levels and tolerance (Gerstein et al., 2007). However, there is considerable evidence to show that onset of diabetes among those with pre-diabetes can be prevented through lifestyle modifications and drug therapy (Echouffo-Tcheugui et al., 2011; Susan van et al., 2010). The Diabetes Prevention Program study, one of the largest randomized control trials looking at the efficacy of lifestyle change for prevention of diabetes, found that risk of developing diabetes for those enrolled in an intensive lifestyle modification intervention decreased by 34% compared to the placebo group (Diabetes Prevention Program Research, 2009). Other studies have similarly found that lifestyle modification, specifically changes in diet and physical activity, and drug therapy can reduce risk for developing diabetes among those with pre-diabetes (Crandall et al., 2008; Gillies et al., 2007; Tuomilehto et al., 2001). Identifying people with prediabetes and diabetes is crucial to linking them, in a timely fashion, to preventive and care services to prevent or delay the onset of disease and to prevent complications from the disease, respectively.

Risk Scores

Screening for Type 2 diabetes is often done using a questionnaire or risk score that measures an individual's likelihood of disease based on the presence or absence of key risk factors like family history of diabetes, hypertension status, and lifestyle (Echouffo-Tcheugui et al., 2011; World Health Organization, 2003). Risk scores are efficient tools for identifying those at highest risk of diabetes and for narrowing down the pool of those that should be offered a diagnostic test (Echouffo-Tcheugui et al., 2011; World Health Organization, 2003). Universal

glucose testing is expensive and may have unwanted negative effects (e.g., psychological harm). As such, targeted testing is more well-accepted, and therefore risk scores offer an efficient avenue, by narrowing in on who should receive a glucose test based on a simple questionnaire-based risk scoring tool. These risk scores are developed using epidemiological data that link exposures to the outcome of Type 2 diabetes (Echouffo-Tcheugui et al., 2011).

Biochemical measures, similar to those used to diagnosis diabetes, can also be used for screening (Echouffo-Tcheugui et al., 2011). Fasting plasma glucose (FPG) and oral glucose tolerance tests (OGTT) are two such tests, but are expensive, and inconvenient for both providers and patients, even for diagnosis (Echouffo-Tcheugui et al., 2011). Given this, it is preferred to only administer these tests to high-risk individuals and not subject individuals to these tests unnecessarily.

Two of the most well-known risk scores in the world are the Finnish Diabetes Risk Score (FINDRISC) and the Canadian Diabetes Risk Assessment (CANRISK). The FINDRISC risk score was developed in Finland to predict the 10 year risk of developing Type 2 diabetes among adults ages 36-54 (Saaristo et al., 2005). The risk score can be self-administered and includes 7 different variables including age, BMI, waist circumference, history of treatment for hypertension and hyperglycemia, physical activity, and fruit/vegetable consumption. These variables are each weighted and the sum of one's cumulative risks is benchmarked against a threshold (or total score) that indicates high risk for diabetes. FINDRISC has been adapted and tested in other populations, particularly in Europe, and has been shown to be an effective predictor of Type 2 diabetes. However, FINDRISC was developed using data from a largely European non-Hispanic white population and so it is not clear that it will perform as well in all

ethnic groups and populations (Janghorbani, Adineh, & Amini, 2013; Kaczorowski, Robinson, & Nerenberg, 2009; Makrilakis et al., 2011; L. Zhang, Zhang, Zhang, Hu, & Chen, 2014).

In order to better account for differences in pathophysiology and prevalence of diabetes across different ethnic groups, researchers in Canada developed and validated the CANRISK questionnaire, which included questions about race and ethnicity, in addition to questions included in FINDRISC (Kaczorowski et al., 2009). The Ministry of Health of Saudi Arabia currently advocates that providers in the Kingdom use an adapted version of the Canadian risk score for diabetes screening. While the CANRISK tool has been validated in numerous cohorts from developed countries, its performance has not yet been assessed in the Saudi population.

Using data from Saudi Arabia, *Memish, et al.* (2015) developed a rapid dysglycemia risk score using only four major risk factors for diabetes: age, history of gestational diabetes, central obesity, and hypertension status. With only four risk factors, this risk score is simpler, more practical, and easier to use, and has been developed “in country.” However, a limitation of this study was that the data was collected using a convenience sample, and has not yet been validated using an external dataset (Memish et al., 2015). If shown to be an effective screening tool, this rapid risk score would be a more efficient, easier-to-administer screening test. With over half of the individuals with diabetes in Saudi Arabia undiagnosed, this is of particular importance (El Bcheraoui et al., 2014).

Using the data available from the 2012 Saudi Household Interview Survey as an external dataset, we assessed the performance of different diabetes/dysglycemia risk scores. Of note, we evaluated a Saudi-specific dysglycemia risk score (Memish et al., 2015), the Finnish (FINDRISC), and Canadian (CANRISK) risk scores. We hypothesized that a diabetes risk score

designed and developed in the Saudi population, albeit using a different dataset, will have higher sensitivity and specificity than the FINDRISC and CANRISK scores.

Problem Statement

The Kingdom of Saudi Arabia is experiencing increasing rates of Type 2 diabetes, with 13.4% of the adult population estimated to have diabetes, half of which do not even know they have the disease (El Bcheraoui et al., 2014; Zabetian et al., 2013). There is a need to identify these individuals through targeted screening, which will require an effective dysglycemia and diabetes risk score that has been validated in the Saudi population. *Memish, et al. (2015)* has developed a rapid, simple dysglycemia risk score using data from Saudi Arabia, based on four major risk factors for diabetes: age, history of gestational diabetes, central obesity, and hypertension status. This risk score is simple, easy to use, and was developed within Saudi Arabia, but has yet to be validated on an external dataset. This risk score can be validated with the data available from the 2012 Saudi Household Interview Survey, a nationally representative, external dataset. Validating this risk score and comparing its performance with other known risk scores (FINDRISC, CANRISK) can help inform the Ministry of Health which score to recommend for use in detecting diabetes risk earlier in the Saudi population.

Purpose Statement:

The purpose of this thesis is to compare the performance of a rapid Saudi-specific dysglycemia risk score, the Finnish (FINDRISC), and Canadian (CANRISK) risk scores, using data from the Saudi Household Interview Survey. Understanding how this rapid Saudi-specific

dysglycemia risk score performs compared to other commonly used risk scores will provide information to help inform the Ministry of Health of the Kingdom of Saudi Arabia, on whether the rapid risk score should be considered for wider use or not.

Research Questions:

1. How does the performance of dysglycemia risk score developed by *Memish, et al. (2015)* as a screening tool (sensitivity, specificity, positive predictive value, negative predictive value, kappa statistic) compare to that of the Finnish and Canadian risk scores?

Significance:

If shown to be an effective screening tool, this rapid risk score would be a more efficient, easier-to-administer screening test. Linking to care and preventive services is critical for the successful management and control of any dysglycemia condition (prediabetes or diabetes) (Sheehy et al., 2009). With over half of the individuals with diabetes in Saudi Arabia undiagnosed, this is of particular importance (El Bcheraoui et al., 2014). Having a validated, simple four question risk score will aid local health professionals in rapidly screening individuals who may be at high risk for diabetes or pre-diabetes and referring those individuals for a diagnostic test (Sheehy et al., 2009). Better screening to identify dysglycemia will allow for more efficient and cost effective targeting of individuals for further diagnostic testing, an important first step for referring individuals for proper and timely diabetes care, prevention, and treatment (Echouffo-Tcheugui et al., 2011; Sheehy et al., 2009; World Health Organization, 2003).

Definition of terms:

Type 2 Diabetes mellitus: a non-auto-immune cardio-metabolic disorder characterized by loss of beta-cell function leading to insulin secretory defect, and reduced insulin sensitivity (American Diabetes Association, 2004).

Pre-diabetes: Also known as borderline-diabetes and can come in the form of impaired fasting glucose (IFG), or impaired glucose tolerance (IGT), or combined IFG-IGT; occurs when blood glucose levels are elevated beyond normal levels, but are not yet meeting the threshold for a diagnosis of diabetes (American Diabetes Association, 2004).

Dysglycemia: Includes both diabetes and prediabetes (Susan van et al., 2010).

Screening: A tool or instrument used to identify individuals at high risk for a disease or condition of interest so they can be referred for diagnostic testing (World Health Organization, 2003).

Risk score: A screening tool in which a formula is developed from epidemiological studies using risk factors for the disease or condition of interest, in order to identify those at high risk that should be referred for diagnostic testing (Echouffo-Tcheugui et al., 2011).

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CHAPTER 2: COMPREHENSIVE REVIEW OF THE LITERATURE

Screening for Type 2 diabetes and dysglycemia is typically done with a questionnaire (or risk score) or with biochemical measurements, such as fasting-plasma glucose (FPG), and oral glucose tolerance test (OGTT). However, the biochemical tests are expensive, and inconvenient for both providers and patients (Echouffo-Tcheugui et al., 2011). For these reasons, questionnaires or risk scores are generally preferred for screening and onerous biochemical testing is reserved for diagnostic testing and targeted (i.e., only those that are at sufficient risk should undergo the tests). Risk scores measure an individual's likelihood of disease based on the presence or absence of key risk factors like family history of diabetes, hypertension status, and lifestyle (Echouffo-Tcheugui et al., 2011; World Health Organization, 2003). They are developed using epidemiological data that link exposures (past medical and family history, lifestyle, anthropometric and demographic information) to the health outcome of diabetes and prediabetes (Echouffo-Tcheugui et al., 2011). Most often this involves creating a prediction model using logistic regression, but can also be done with prediction methods such as decision trees (Barber, Davies, Khunti, & Gray, 2014; Thooputra, Newby, Schneider, & Li, 2012). Individuals are given a score based on their exposures to risk factors, indicating whether or not further diagnostic testing is needed (World Health Organization, 2003).

There is no single global standard dysglycemia risk score. As diabetes prevalence rises globally, there have been concerns that screening tools should be context-specific; i.e., the tools should perform adequately in different ethnic and geographic groups and also incorporate risk factors that may be unique (Thooputra et al., 2012). With strong evidence of the effectiveness of lifestyle interventions to prevent the onset of diabetes among high-risk

individuals, there has been a shift in focusing on detecting dysglycemia, which includes prediabetes and diabetes (Diabetes Prevention Program Research, 2009; Thoopputra et al., 2012).

The majority of risk scores have been developed in North America and Europe (Thoopputra et al., 2012). If existing risk scores are to be used in other populations, there is a need to validate those risk scores in the target populations they will be implemented in. Some studies have validated existing risk scores on external datasets using cohort or cross-sectional data. Alternatively, some studies have looked to develop population-specific risk scores, using data from the target population to develop a risk score tool. This section will detail studies validating two of the most commonly used risk scores globally, the Finnish Diabetes Risk Score (FINDRISC) and the Canadian Diabetes Risk Score (CANRISK), followed by a discussion of risk scores that have been developed and validated in the gulf countries (Oman, Kuwait, Bahrain, United Arab Emirates, Saudi Arabia, and Qatar).

Measure for validating risk score performance

Sensitivity, specificity, positive predictive value, and negative predictive value are commonly used to assess the accuracy of a diagnostic test. In the case of screening for diabetes, these measures help assess the accuracy of the risk score in identifying those who truly have diabetes and should be referred for further diagnostic testing from those who do not have diabetes.

Sensitivity is a measure of how well the risk score detects true disease (true positives) and is the probability that an individual is accurately classified as having the disease by the risk

score given he or she actually has the disease. A higher sensitivity means that a test is better at identifying those that truly have the disease, and is less likely to have false negatives (individuals with the disease classified as not having the disease). Sensitivity is calculated as the number of people with the disease classified as having the disease divided by the total number of people classified as having the disease, whether they truly have the disease or not.

Specificity is the measure of how well the risk score detects individuals who do not have the disease (true negatives) and is the probability that an individual is accurately classified as not having the disease given he or she truly does not have the disease. A higher specificity means that a test is better at correctly identifying those who do not have the disease, and is less likely to have false positives (individuals who do not have the disease classified as having the disease). Specificity is calculated as the number of individuals classified as not having the disease who truly do not have the disease divided by the total number of individuals classified as having not having the disease, whether they truly do not have the disease or not.

Positive predictive value (PPV) is the probability that those who are predicted to have the disease truly have the disease. A higher PPV indicates that the test is efficient and there is a high probability that someone who is predicted to have the disease actually has the disease. PPV is calculated as the number of individuals predicted to have the disease that truly have the disease divided by the total number of individuals predicted to have the disease. Negative predictive value (NPV) is the probability that those predicted to not have the disease truly do not have the disease. NPV is calculated as the number of individuals predicted to not have the disease who truly do not have the disease divided by the total number of individuals predicted to not have the disease.

The receiver operating characteristic (ROC) curve is a graph of sensitivity plotted against 1 - specificity. The area underneath this curve (AUC) is a measure of the test's ability to accurately identify those with the disease from those without the disease. An AUC of 1 indicates the test is perfectly accurate, while an AUC of 0.5 indicates the test's ability to correctly identify those with the disease from those without the disease is no better than chance. Generally, an AUC between 0.7 and 0.9 indicates that a test is moderately accurate (Thoopputra et al., 2012).

The kappa statistic for agreement can be used to assess the cumulative frequency of the risk scores' predicting dysglycemia when true dysglycemia was present, and no dysglycemia when true dysglycemia was not present. The kappa statistic is the measure of the difference between how much agreement is observed and how much agreement would be expected given chance alone. Kappa statistics can range from -1 to 1. A score of 1 indicates perfect agreement, or perfect prediction of dysglycemia in the population. A score of 0 is what we would expect if all agreement was a result of chance. A score ranging from 0.01 to 0.2 indicates slight agreement, from 0.21 to 0.4, fair agreement (Viera & Garrett, 2005).

Known risk scores

FINDRISC

The Finnish Diabetes Risk Score or FINDRISC, was developed in Finland to predict the 10 year risk of developing Type 2 diabetes among adults ages 36-54 (Saaristo et al., 2005). The risk score can be self-administered and includes 7 different variables including age, BMI, waist circumference, history of treatment for hypertension and hyperglycemia, physical activity, and

fruit/vegetable consumption. The risk score performed well, with a sensitivity and specificity of 77% and 78% respectively (Lindstrom & Tuomilehto, 2003).

FINDRISC is commonly used globally and has been shown to be an effective predictor of Type 2 diabetes and dysglycemia in countries including Greece (Makrilakis et al., 2011), Germany (Bergmann et al., 2007), the Netherlands (Alsema et al., 2008), Italy (Bonaccorsi, Guarducci, Ruffoli, & Lorini, 2012), Mexico (Garcia-Alcala, Genestier-Tamborero, Hiraes-Tamez, Salinas-Palma, & Soto-Vega, 2012), Bulgaria (Tankova, Chakarova, Atanassova, & Dakovska, 2011) Iran (Janghorbani et al., 2013), the United States (L. Zhang et al., 2014), and Taiwan (Lin et al., 2009). However, FINDRISC was developed using data from a largely European non-Hispanic white population, so it is not clear that it will perform as well in all ethnic groups and populations (Kaczorowski et al., 2009). A study in Southern Spain found that FINDRISC did not perform as well at detecting diabetes compared to the PREDIMED-clinical score, which was developed from data from a randomized, controlled trial conducted in Spain to assess benefits of the Mediterranean diet to prevent cardiovascular events and mortality (Guasch-Ferré et al., 2012).

CANRISK

In order to better account for differences among different ethnic groups, Canada developed and validated the CANRISK questionnaire, which included questions about gender, race and ethnicity, and education level, in addition to questions included in FINDRISC. This risk score used population-based data from Canada and was designed to be a self-administered questionnaire that would detect undiagnosed Type 2 diabetes, IGT, or IFG within the Canadian

population (Kaczorowski et al., 2009). CANRISK was validated in a pooled epidemiologic study with population-based data from seven provinces with multi-ethnic populations (Robinson, Agarwal, & Nerenberg, 2011). The study found that CANRISK was more accurate than FINDRISC and a simplified obesity model (variables: age, BMI, waist circumference, and sex) in detecting undiagnosed diabetes and prediabetes, with AUCs of 0.75, 0.66 and 0.65 respectively. A study looking at high-risk communities in Toronto also found CANRISK to perform well in detecting diabetes and prediabetes in multi-ethnic populations (AUC=0.716) (Rowan et al., 2014).

An Arabic version of CANRISK called ARABRISK has been adapted to be used in Arabic-speaking countries. ARABRISK contains the same questions as CANRISK, which have been translated to Arabic (Alghwiri, Alghadir, & Awad, 2014). The Ministry of Health of Saudi Arabia currently recommends using ARABRISK for diabetes and prediabetes screenings. A study was done in Jordan and Riyadh, Saudi Arabia found that the scores calculated using ARABRISK were significantly correlated with fasting plasma glucose levels (Pearson correlation coefficient, $r=0.3$, $p=0.01$) (Alghwiri et al., 2014). This study did not use diabetes or prediabetes as an outcome, and thus did not look at how well ARABRISK performed in predicting the health outcomes of diabetes or prediabetes.

Gulf Countries

The gulf countries include Oman, Kuwait, Bahrain, United Arab Emirates, the Kingdom of Saudi Arabia, and Qatar. In addition to their close proximity to each other, these countries share similarities in their history, culture, political landscape, and economic development. They are all part of the Middle East and North Africa region, which has recently been found to have

the second highest prevalence of diabetes in the world, second only to Polynesia and Micronesia (NCD Risk Factor Collaboration, 2016).

Kingdom of Saudi Arabia

There have been two risk scores developed in Saudi Arabia. The first was developed in 2013 to detect individuals with undiagnosed diabetes (Handlos et al., 2013). The risk score was developed using a cross-section study design, recruiting participants from Jeddah and Riyadh through convenience sampling. A total of 2,446 adults aged 30-75 participated in this study, including Arabs and non-Arabs. The study excluded individuals with a previous diagnosis of diabetes and pregnant women, and 86.1% of the study population was Arab. Having diabetes was defined as having a HbA1c $\geq 6.5\%$. Stepwise backward elimination was used to develop a risk score for undiagnosed diabetes that included age, gender, BMI, gestational diabetes, ethnicity, and number of siblings with diabetes. The diabetes risk score had a sensitivity of 74% [67-81%] and a specificity of 52% [49-54%]. The risk score for dysglycemia contained the same variables as its risk score for diabetes, except for male and ethnicity. The sensitivity and specificity of the dysglycemia risk score was 74% [70-78%], 55% [53-57%], respectively. Neither risk score was not validated. The weak study design and lack of external validation limits the generalizability to the Saudi population as a whole.

In 2015, *Memish, et al.* developed risk scores to detect diabetes and dysglycemia, using data from collected from 1,435 Saudi adults, 20 years of age or older (Memish et al., 2015). Pregnant women and those with a current diagnosis of diabetes were excluded. Data was collected through convenience sampling at urban and rural primary healthcare centers in 2009.

The outcome of diabetes was defined as fasting plasma glucose ≥ 7.0 mmol/L or 2-h post-load glucose ≥ 11.1 mmol/L. The outcome of dysglycemia was defined as fasting plasma glucose ≥ 5.6 mmol/L or 2-h post-load glucose ≥ 7.8 mmol/L. The risk scores were developed using stepwise, forward, and backward logistic regression and were internally validated in a smaller hold-out sample. The final risk score for detecting diabetes included five variables: age, history of gestational diabetes, smoking, family history of diabetes, and central obesity. The diabetes risk score had a sensitivity of 76.6% [70.3–81.9%] and a specificity of 52.1% [49.3–54.9%]. The final risk score for detecting dysglycemia (both diabetes and prediabetes) included four variables: age, history of gestational diabetes, central obesity, and hypertension status. The dysglycemia risk score had a sensitivity of 71.2% [67.6–74.6%] and a specificity of 54.0% [50.3–57.6%]. Both risk scores performed better in the validation holdout samples. Interestingly, the risk score to predict dysglycemia contained fewer variables and did not include smoking status or family history of diabetes, which found to be a strongly associated with diabetes (Echouffo-Tcheugui et al., 2011). Also, of note, the dysglycemia risk score did include hypertension status, while the diabetes risk score did not. Limitations of this study include the cross-sectional design, use of convenience sampling, and lack of validation with an external dataset.

United Arab Emirates

Handlos, et al. also developed risk scores for diabetes and dysglycemia for the United Arab Emirates (UAE), using the same method as the diabetes risk score they developed for Saudi Arabia (Handlos et al., 2013). The study population included 1,987 individuals from the cities of Sharjah, Dubai, and Abu Dhabi. For this analysis, 45.3% of the study population was

Arab. Data was collected through convenience sampling and the risk score developed using stepwise backward elimination. The final model for the UAE diabetes risk score included four variables: age, BMI, gender, and ethnicity. The sensitivity for this risk score was 73% [66-79%], and specificity, 55% [53-58%]. The risk score for dysglycemia contained the same variables as its diabetes risk score, a sensitivity of 78% [73-82%], and specificity of 52% [50-55%].

Oman

A diabetes risk score was developed in Oman in 2007, using data from the 1991 National Diabetes Survey (Al-Lawati & Tuomilehto, 2007). A total of 4,881 Omani adults, 20 years of age or older, were included in this study. Pregnant women and those with diabetes who showed their diabetes medications to the researchers were excluded. The outcome of diabetes was defined by a 2hrPPG \geq 200 mg/dL. The risk score was developed using backward stepwise logistic regression and included five variables: age, waist circumference, BMI, family history of diabetes, and current diagnosis of hypertension. The Omani diabetes risk score had a sensitivity of 78.6% [74.6-82.1%] and a specificity of 73.4% [72-74.7%]. The risk score was validated using data from a 2001 cross-sectional study, and performed well in the validation sample, with a sensitivity of 62.8% [54.3-70.6%] and specificity of 78.2% [75.8-80.4%].

Kuwait

A diabetes risk score was developed in Kuwait in 2010 using data from a cross-sectional study (Al Khalaf, Eid, Najjar, Alhajry, & Thalib, 2010). In this study, data was collected from 460 government employees using multi-stage cluster sampling, excluding pregnant women and

those previously diagnosed with diabetes. The outcome of diabetes was defined using the American Diabetes Association's definition of FPG ≥ 126 mg/dL or random plasma glucose ≥ 200 mg/dL. The risk score was developed using forward stepwise logistic regression and the final model included four variables: age, waist circumference, treatment for hypertension, and presence of a sibling with diabetes. The risk score had a sensitivity of 87% and specificity of 64%, but was not validated. When the authors tested the Omani diabetes risk score on this population, they found that the Omani risk score was more sensitive (96%), but less specific (42%). This was different than how the Omani diabetes risk score performed in the Omani population, suggesting the importance of validating risk scores in each target population. Since this study only included individuals who worked for the government, the results may not be generalizable to the greater adult population in Kuwait.

Conclusion

The majority of diabetes and dysglycemia risk scores have been developed in North America and Europe (Thoopputra et al., 2012). However, as the burden of diabetes grows worldwide, there is an increasing need to validate risk scores in new target populations or to develop new risk scores specific to their target population. There are a few risk scores that have been developed in the gulf countries. However, these risk scores used cross-sectional designs and convenience sampling, limiting the validity and applicability of these risk scores for the wider target population. There is a need to validate these risk scores, especially with external datasets.

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CHAPTER 3: MANUSCRIPT

ABSTRACT

Objective: To assess the performance of three diabetes risk scores: a rapid Saudi-specific dysglycemia risk score, the Finnish Diabetes Risk Score (FINDRISC), and the Canadian Diabetes Risk Assessment (CANRISK) as a screening tool for dysglycemia, using data from the Saudi Household Interview Survey, a recent nationally representative cross-sectional study in Saudi Arabia.

Research Design and Methods: Data from 4,461 Saudi adults aged 15 years or older who participated in the Saudi Health Interview Survey and completed an HbA1c lab test were included in the analysis. Anthropologic measurements, socio-demographic information, lifestyle information, and past medical history were collected through household surveys. Participants were referred to a local clinic to complete biochemical measurements, including HbA1c. We assessed the performance of a Saudi-specific risk score, the FINDRISC, and CANRISK tools by calculating sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). We also estimated the kappa statistic for agreement for each risk score to assess the frequency of the risk scores predicting dysglycemia when true dysglycemia was present, and no dysglycemia when true dysglycemia was not present.

Results: Overall, CANRISK was the most sensitive in identifying those with dysglycemia (CANRISK: 70.57% [70.54, 70.59] vs. Saudi-specific score: 53.58% [51.36, 55.80] vs. FINDRISC: 39.46% [39.43, 39.49]), but the least specific in detecting those without dysglycemia (CANRISK: 55.87% [55.85, 55.89] vs. Saudi-specific score: 75.54 [73.86, 77.21] vs. FINDRISC: 82.95 [82.83, 82.86]). The PPV was similar among the three risk scores, ranging from 55.2%–63.9%. The NPV was also similar among the three risk scores, ranging from 64.0%–71.2%. The Saudi-specific score had the highest kappa statistic (Saudi-specific score: 0.296, se=0.014; CANRISK: 0.260, se=0.015; FINDRISC=0.233, se=0.014) and demonstrated the best balance in correctly detecting individuals with and without dysglycemia. All three risk scores performed better in identifying individuals with diabetes, compared to identifying individuals with dysglycemia. All three risk scores did not perform as well when detecting undiagnosed dysglycemia and undiagnosed diabetes.

Conclusion: Based on our analysis, the rapid Saudi-specific dysglycemia risk score performs as well as the FINDRISC and CANRISK.

INTRODUCTION:

The Middle East and North Africa (MENA) region has the second highest comparative rates of diabetes in the world, second only to Polynesia and Micronesia (NCD Risk Factor Collaboration, 2016). According to the International Diabetes Federation Atlas, 35.4 million adults were estimated to be affected by diabetes in the MENA region in 2015, with that number projected to double by 2040 (International Diabetes Federation, 2015). It appears that increases in diabetes in this region are occurring parallel to economic development, rapid urbanization, and may be related to increasingly sedentary lifestyles, poor diet, and increased life expectancy (Anokute, 1990; Murad et al., 2014; Sherif & Sumpio, 2015).

Type 2 diabetes is a growing health concern for the Kingdom of Saudi Arabia. Numerous studies have been done to measure the prevalence of diabetes in the country. A systematic review of such studies found that diabetes prevalence ranged from 2.5% in 1982 to as high as 31.6% in 2011 (Zabetian et al., 2013). In order to support data-driven decision-making and to generate less variable estimates regarding diabetes status in Saudi Arabia, in 2012 the Ministry of Health of Saudi Arabia conducted the Saudi Health Interview Survey (SHIS), a national cross-sectional survey of individuals aged 15 years or older. SHIS used multistage sampling to recruit a population sample that was considered representative of the country's residents. Preliminary findings from this data suggest that 13.4% of the adult population in Saudi Arabia has diabetes, with more than half of those with diabetes undiagnosed (El Bcheraoui et al., 2014). The same study also estimated that 15.2% of the adult population had borderline diabetes or prediabetes. The proportion of individuals with borderline diabetes that were aware of their condition was not reported. However, given data from the United States that found only 11.1%

of individuals with borderline diabetes were aware of their status, this is likely to be low in Saudi Arabia as well (Centers for Disease Control and Prevention, 2013). With a large proportion of those with diabetes and borderline are undiagnosed, there is a need to effectively screen for individuals with diabetes and prediabetes in Saudi Arabia (El Bcheraoui et al., 2014).

Identifying people with prediabetes and diabetes is crucial to linking them, in a timely fashion, to preventive and care services to prevent or delay the onset of disease, and to prevent complications from the disease. Individuals with borderline or prediabetes have a five to ten times higher annual risk of developing diabetes compared to people with normal glucose levels and tolerance. (Gerstein et al., 2007). However, there is considerable evidence to show that onset of diabetes among those with pre-diabetes can be prevented through lifestyle modifications and drug therapy (Crandall et al., 2008; Diabetes Prevention Program Research, 2009; Echouffo-Tcheugui et al., 2011; Gillies et al., 2007; Susan van et al., 2010; Tuomilehto et al., 2001). Furthermore, there is considerable and robust evidence regarding the efficacy of interventions to prevent complications among people with diabetes, through adherence to healthy lifestyle choices (e.g., avoiding tobacco use) and medications to manage glucose, blood pressure, and cholesterol (Chalmers & Arima, 2009; Cholesterol Treatment Trialists, 2015; Mohiuddin et al., 2007; Nathan et al., 2005; Tandon et al., 2012; UK Prospective Diabetes Study (UKPDS) Group, 1998). This is especially important given diabetes is a leading cause of adult-onset blindness, renal failure, and non-traumatic lower limb amputation worldwide (Echouffo-Tcheugui et al., 2011; Susan van et al., 2010).

Risk scores are efficient tools for identifying those at highest risk of diabetes and for narrowing down the pool of those that should be offered a diagnostic test (World Health

Organization, 2003). Universal glucose testing is expensive and may have unwanted negative effects (e.g., psychological harm). As such, targeted testing is more well-accepted, and therefore risk scores offer an efficient avenue, by narrowing in on who should receive a glucose test based on a simple questionnaire-based risk scoring tool.

The most well-known and commonly used risk score globally is the Finnish Diabetes Risk Score (FINDRISC). This risk score was developed in Finland to predict the 10 year risk of developing Type 2 diabetes among adults ages 36-54 (Saaristo et al., 2005). The risk score can be self-administered and includes 7 different variables including age, BMI, waist circumference, history of treatment for hypertension and hyperglycemia, physical activity, and fruit/vegetable consumption. These variables are each weighted and the sum of one's cumulative risks is benchmarked against a threshold (or total score) that indicates high risk for diabetes. FINDRISC has been adapted and tested in other populations, particularly in Europe, and has been shown to be an effective predictor of Type 2 diabetes. However, FINDRISC was developed using data from a largely European non-Hispanic white population, and so it is not clear that it will perform as well in all ethnic groups and populations (Janghorbani et al., 2013; Kaczorowski et al., 2009; Makrilakis et al., 2011; L. Zhang et al., 2014).

In order to better account for differences in pathophysiology and prevalence of diabetes across different ethnic groups, researchers in Canada developed and validated the CANRISK questionnaire, which included questions about race and ethnicity, in addition to questions included in FINDRISC (Kaczorowski et al., 2009). The Ministry of Health of Saudi Arabia currently advocates that providers in the Kingdom use an adapted version of the Canadian risk score for

diabetes screening. While the CANRISK tool has been validated in numerous cohorts from developed countries, its performance has not yet been assessed in the Saudi population.

Using data from Saudi Arabia, *Memish, et al.* (2015) developed a rapid dysglycemia risk score using only four major risk factors for diabetes: age, history of gestational diabetes, central obesity, and hypertension status. With only four risk factors, this risk score is simpler, more practical, and easier to use, and has been developed “in country.” However, a limitation of this study was that the data was collected using a convenience sample, and has not yet been validated using an external dataset (*Memish et al., 2015*). If shown to be an effective screening tool, this rapid risk score would be a more efficient, easier-to-administer screening test. With over half of the individuals with diabetes in Saudi Arabia undiagnosed, this is of particular importance (*El Bcheraoui et al., 2014*).

Using the data available from the 2012 Saudi Household Interview Survey as an external dataset, we assessed the performance of different diabetes/dysglycemia risk scores. Of note, we evaluated a Saudi-specific dysglycemia risk score (*Memish et al., 2015*), the Finnish (FINDRISC), and Canadian (CANRISK) risk scores. We hypothesized that a diabetes risk score designed and developed in the Saudi population, albeit using a different dataset, will have higher sensitivity and specificity than the FINDRISC and CANRISK scores.

METHODS

Data Source

We analyzed data from the Saudi Health Interview Survey (SHIS), a cross-sectional survey of individuals aged 15 or older in the Kingdom of Saudi Arabia. The survey was conducted in 2012 by the Ministry of Health of the Kingdom of Saudi Arabia and the Institute for Health Metrics and Evaluation (IHME). The purpose of the survey was to assess chronic disease, health behaviors, and risk factors among Saudi adults aged 15 years or older.

Study Design and Data Collection

SHIS used complex multistage probability cluster sampling to ensure adequate representation of the adult Saudi population across the country. Trained interviewers conducted household interviews, collecting data on demographics, medical history, and lifestyle behaviors using questionnaires, and conducted standardized anthropometric measurements (e.g., weight, height). Participants were referred to local clinics for fasting blood draws once the initial questionnaire was complete. After blood was drawn from the participant, the local clinic shipped the collected blood sample to King Fahd Medical City (KFMC) in Riyadh for analysis. This was done to ensure all laboratory methods were standardized. The blood collected was tested for fasting lipid profile, glycated hemoglobin (HbA1c), and Vitamin D.

The response rate for the household section of the survey was 90%, with 49.5% of all participants also completing the lab section of the survey. Detailed methodology regarding the study design, sampling, and data collection are reported elsewhere (El Bcheraoui et al., 2014).

Study Variables

The variables used in these analyses are described and defined in further detail below.

Outcomes

The presence of diabetes was defined based on the Saudi National Diabetes guidelines: self-reported diagnosis of diabetes or HbA1c \geq 6.5% (Ministry of Health, 2014). Presence of prediabetes was assessed according to self-report diagnosis of prediabetes or HbA1c of 5.7-6.4% (Ministry of Health, 2014). Dysglycemia refers to the presence of either diabetes or prediabetes.

Exposures

The Saudi-specific risk score developed by *Memish, et al.* contains four predictor variables: age, gestational diabetes, hypertension, and waist circumference, with a total possible score ranging from 0 – 21 points. Table 1 shows how each exposure variable was defined and weighted for each risk score. The Finnish risk score contains eight predictor variables: age, body mass index, family history of diabetes, waist circumference, use of anti-hypertensive medication, history of elevated blood glucose, daily physical activity and daily consumption of fruit and vegetables, with a total possible score ranging from 0 – 27 points. The Canadian risk score contains the eight variables used in the Finnish risk score in addition to macrosomia, gender, race, and education level, with a total possible score ranging from 0 – 72 points (Memish et al., 2015; Finnish Diabetes Association; Public Health Association of Canada, 2011). In order to calculate each participant's risk using the SHIS data, all continuous variables were converted into categorical variables, so they could be assigned a score. The scores of each

individual risk factor were added together to come up with an overall risk score. This was done for all three risk scores. Risk factors used in our analyses and their original classification in the SHIS data are described below in greater detail.

Demographic factors: Age strata were defined differently for each risk score, and treated as a categorical variable. Sex was analyzed as “Male” or “Female” based on observation of the interviewer. Highest education level obtained was re-categorized as “completed high school”, “completed university or graduate level degree”, and “have not completed high school”. Since the study was limited to participation by Saudi nationals, race for all participants was classified as Saudi or Arab.

Lifestyle factors: Physical activity was analyzed as a dichotomous variable, defined as being active for at least 30 minutes a day (or 210 minutes per week) or not. This included moderate and vigorous physical activity for both work and recreational purposes. Self-reported data regarding the number of days and minutes spent being physically active in an average week was used for this analysis. Fruit and vegetable consumption was also analyzed as a dichotomous variate, defined as consumption of any amount of fruits and vegetables every day or not. Self-reported average number of days per week of fruit consumption and average number of days per week of vegetable consumption were summed for this analysis.

Anthropometric factors: Body mass index (BMI, kg/m^2) and waist circumference (WC, cm) were classified into categories as defined by each risk score and treated as categorical variables.

Medical and family history: Medical history of hypertension, gestational diabetes, and family history of diabetes, were analyzed as dichotomous exposures: either “present” or “not

present”. Presence of hypertension was defined as self-reported diagnosis of hypertension or blood pressure measurements using National Heart Association guidelines (if systolic ≥ 140 mmHg or diastolic ≥ 90 mmHg) (Memish et al., 2015). History of gestational diabetes and family history of diabetes were determined based on self-report data.

In the SHIS survey, presence of family history of diabetes mellitus (parents, siblings, and offspring) was only collected for those who positively responded that they had been diagnosed with diabetes. This resulted in missing data for family history of diabetes for those who had not been diagnosed with diabetes. Because family history is a component of both the FINDRISC and Canadian risk score, family history of diabetes was imputed using multiple imputations. We randomly generated a value for family history of diabetes, “Yes” or “No”, based on the predictive probability of that individual having answered “Yes”. The predicted probability was calculated using a regression model developed and validated among observations that did have a response for family history. The model to classify family history included age, marital status, sex, and highest level of education. The imputation was run ten times to account for variability between imputations. For all analysis involving FINDRISC and CANRISK, the average value of the ten imputations was reported.

Data Cleaning

For all variables, “don’t know” and “declined to respond” were coded as missing.

Known diabetes risk calculators and associated variables

This section details the harmonization of how risk factors are defined by each risk score and how they are collected in the SHIS survey. Further details on variable harmonization can be found in Table 1. For the Saudi-specific risk score, presence of hypertension was defined by self-report or blood pressure measurements using National Heart Association guidelines (if systolic ≥ 140 mmHg or diastolic ≥ 90 mmHg) (Memish et al., 2015). For FINDRISC and CANDRISK, presence of hypertension was defined by self-report only (Finnish Diabetes Association; Public Health Agency of Canada, 2011).

Family history of diabetes was defined as a history of diabetes in any parent, child, or sibling. For FINDRISC, any presence of family history of diabetes was counted with the same weight in the risk score. For CANDRISK, the number of family members with a history of diabetes had a cumulative effect on the risk score. However, since the number of family members with history of diabetes was not collected in SHIS, we could not take into account this cumulative effect. In our analysis, for individuals with a family history of diabetes, we assigned them the value of having one family member with a history of diabetes for their CANDRISK score, since we could not be sure if multiple family members had a history of diabetes.

CANDRISK also includes a question on history of macrosomia, or having given birth to a large baby weighing 9 pounds or more. History of macrosomia was not asked as part of SHIS. Gestational diabetes was used as a proxy for macrosomia in this analysis.

Data Analysis

Data was analyzed using SAS[®] software version 9.4 (SAS Institute Inc., Cary, NC). A total of 10,821 individuals participated in the SHIS study. However, only individuals (n= 4,461) who had completed the lab portion of the survey were included in the analysis. Predicted dysglycemia was determined based on the cutoff values for moderate to high risk of developing prediabetes and diabetes in each of the risk scores: *Saudi-specific score* > 9, out of a maximum of 21 points; FINDRISC > 12, out of a maximum of 27 points; CANRISK > 21, out of a maximum of 72 points (Rowan et al., 2014; Y. Zhang, Hu, Zhang, Mayo, & Chen, 2015). If the risk score for an individual was above the cutoff, the variable predicted dysglycemia was coded as “Yes”. If the risk score was below the cutoff, predicted dysglycemia was coded as “No”. Individuals with true dysglycemia were defined as individuals who reported they had been diagnosed with diabetes or prediabetes, and individuals with HbA1c \geq 5.7%.

To assess the performance of each risk score, we calculated standard measures of sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). Sensitivity is the proportion of those who have the disease that test positive, while specificity is the proportion of those who do not have the disease that test negative. Positive predictive value is the proportion of those who test positive that actually have the disease, while negative predictive value is the proportion of those who test negative that actually do not have the disease.

We also estimated the kappa statistic for agreement for each risk score to assess the cumulative frequency of the risk scores’ predicting dysglycemia when true dysglycemia was present, and no dysglycemia when true dysglycemia was not present. The kappa statistic is the

measure of the difference between how much agreement is observed and how much agreement would be expected given chance alone. Kappa statistics can range from -1 to 1. A score of 1 indicates perfect agreement, or perfect prediction of dysglycemia in the population. A score of 0 is what we would expect if all agreement was a result of chance. A score ranging from 0.01 to 0.2 indicates slight agreement, from 0.21 to 0.4, fair agreement (Viera & Garrett, 2005).

For the primary analysis, we used dysglycemia as the main outcome of interest and assessed the performance of the risk scores in detecting all individuals with dysglycemia, including those that had been diagnosed with diabetes or prediabetes. We then removed individuals that had been diagnosed with diabetes or prediabetes to assess how the risk scores performed for detecting undiagnosed dysglycemia. This analysis was repeated using diabetes as the outcome of interest, to see if the risk scores performed better at detecting diabetes compared to dysglycemia.

RESULTS

Table 2 shows the characteristics of the participants that completed laboratory testing and were included in the analysis ($n=4,461$). Mean age was 39.56 years ($sd=16.69$). The majority of participants were female (52.3%) and reported that they had completed high school or a higher degree (51.8%). Mean BMI for participants was 28.5 kg/m^2 ($sd=6.58$). Approximately 51.1% of participants reported eating any fruits and vegetables every day, and 9.6% reported engaging in 30 minutes of moderate to vigorous physical activity every day.

When asked if they had ever received a diagnosis of diabetes from a healthcare provider, 13.7% of participants responded “yes”. An additional 2.6% reported they had been diagnosed with borderline diabetes or prediabetes by a healthcare provider. Of the participants included in this analysis, 16.5% had an HbA1c \geq 6.5, and 39.3% had an HbA1c \geq 5.7%.

Table 3 provides estimates of sensitivity, specificity, PPV, and NPV (and respective 95% CI's) for each of the three risk scores used. Overall, CANRISK was the most sensitive in identifying those with dysglycemia (CANRISK: 70.57% [70.54, 70.59] vs. Saudi-specific score: 53.58% [51.36, 55.80] vs. FINDRISC: 39.46% [39.43, 39.49]), but the least specific in detecting those without dysglycemia (CANRISK: 55.87% [55.85, 55.89] vs. Saudi-specific score: 75.54 [73.86, 77.21] vs. FINDRISC: 82.95 [82.83, 82.86]). The PPV was similar among the three risk scores, ranging from 55.2%–63.9%. The NPV was also similar among the three risk scores, ranging from 64.0%–71.2%.

The kappa statistic can be used to assess the level of agreement between the risk score predictions and the actual presence or absence of dysglycemia based on self-report diagnosis and HbA1c scores. The Saudi-specific risk score had the highest kappa statistic of the three risk scores (Saudi-specific score: 0.296, se=0.014; CANRISK: 0.260, se=0.015; FINDRISC=0.233, se=0.014) and demonstrated the best balance in correctly detecting individuals with and without dysglycemia. Thus, the predictions from the Saudi-specific score, tended to agree with the actual status of dysglycemia more than CANRISK and FINDRISC.

The same analysis was done after removing any participants that had been diagnosed with dysglycemia, defined as having been previously diagnosed with diabetes or prediabetes (Table 4). For all three risk scores, sensitivity decreased by a range of 6-12 percentage points when

detecting undiagnosed dysglycemia. CANRISK remained the most sensitive risk score, while specificities for all three risk scores remained largely unchanged. The PPV of all three risk scores decreased by an average of 16.5 percentage points, while the NPV of all three risk scores increased by an average of 4.2 percentage points.

Table 5 shows the mean scores for each risk score by gender (female, male) and dysglycemia status (diabetes, prediabetes). For all three risk scores, the score did not vary significantly by gender or dysglycemia status. When looking at the mean values relative to the cutoff scores for dysglycemia, for the Saudi-specific score the mean score for women, men, and individuals with prediabetes was lower than the cutoff score of 8. Appropriately, the mean score for individuals with diabetes was above the cutoff score. For FINDRISC, the mean scores were below than the cutoff score of 12 for all categories of participants (male, female, prediabetes, diabetes). For CANRISK, the inverse was true as all categories of participants had mean scores that were above the cutoff value of 21.

Table 6 shows the diagnostic performance of each risk score broken down by gender. When analyzing males and females separately, CANRISK remained the most sensitive risk score and FINDRISC the most specific for both males and females. The Saudi-specific risk score was the most balanced risk score, with the highest kappa statistics for both females and males. Looking at differences between genders within each risk score, for the Saudi-specific score, the sensitivity and specificity was similar for males and females, with males having a slightly higher PPV and lower NPV compared to females. For FINDRISC, the risk score was more sensitive for females and more specific for males, with males having a higher PPV and lower NPV compared to females. For CANRISK, the risk score was more sensitive for males and more specific for

females, with males also having a higher PPV. For CANRISK, there was no difference in NPV between males and females.

Table 7 shows the diagnostic performance of each risk score for detecting diabetes to see how the risk score performs in identifying the highest risk individuals. All three risk scores performed better in identifying individuals with diabetes, compared to identifying individuals with diabetes and prediabetes. For all three scores, sensitivity was higher by an average of 11.5 percentage points, with the Saudi-specific score seeing the largest difference. For all three scores, PPV was lower by an average of 22 percentage points, while NPV was higher by an average of 20 percentage points. The Saudi-specific score again was the most balanced risk score for detecting diabetes, with the highest kappa statistic of all three risk scores (Saudi-specific score: Kappa=0.3141, sd=0.0143; FINDRISC: Kappa=0.2843, sd=0.0165; CANRISK: Kappa=0.2145, sd=0.0112).

A similar trend was found for detecting diabetes among those without diagnosed diabetes (Table 8). The risk scores were more sensitive when detecting undiagnosed diabetes compared to undiagnosed dysglycemia. Again, PPV was significantly lower while NPV was significantly higher for all three risk scores compared to detecting undiagnosed dysglycemia. The kappa statistics were significantly lower for all three risk scores, with the Saudi-specific score again having the highest kappa statistic of the three risk scores (Saudi-specific score: Kappa=0.0981, sd=0.0256; FINDRISC: Kappa=0.0816, sd=0.0169; CANRISK: Kappa=0.0725, sd=0.0095).

DISCUSSION:

Using data from a nationally representative survey, we assessed the ability of three different dysglycemia risk scores to accurately identify Saudi nationals with dysglycemia. For this analysis we compared a risk score developed using data from Saudi Arabia (Memish et al., 2015) with the Finnish Diabetes Risk Score (FINDRISC) and Canadian risk assessment for diabetes (CANRISK).

In our analysis, we found that CANRISK was consistently the most sensitive risk score and better at detecting true dysglycemia than both the FINDRISC and Saudi-specific scores. However, CANRISK also had the lowest specificity of all three risk scores. Conversely, FINDRISC did not perform well in detecting true dysglycemia and was consistently the least sensitive risk score for detecting dysglycemia and undiagnosed dysglycemia. The Saudi-specific score provided the best balance of sensitivity and specificity for detecting dysglycemia and had the highest kappa statistic for detecting dysglycemia and undiagnosed dysglycemia. All three risk scores were better at predicting all dysglycemia, compared to only undiagnosed dysglycemia.

All three scores were more sensitive for detecting diabetes than dysglycemia, with CANRISK remaining the most sensitive, and the Saudi-specific score having the highest kappa statistic of the three risk scores. The Saudi-specific score had a higher kappa statistic for detecting diabetes compared to dysglycemia, suggesting that the risk score, while designed to detect dysglycemia, may actually be better at detecting diabetes.

The sensitivities and specificities of the CANRISK and Saudi-specific scores, were similar to what has been reported from other risk scores developed in other gulf countries, including Oman, Kuwait, the United Arab Emirates, and Saudi Arabia (Al-Lawati & Tuomilehto, 2007; Al

Khalaf et al., 2010; Handlos et al., 2013). FINDRISC performed poorly in this population, especially given when validated in the Finnish population, FINDRISC had a sensitivity and specificity of 77% and 78%, respectively.

An interesting finding was that for CANRISK, the mean scores for all groups of participants (men, women, those with prediabetes, and those with diabetes) were above the cutoff value, while for FINDRISC, none of the groups had a mean score above the cutoff value. For the Saudi-specific score, only those with diabetes had a mean score above the cutoff value. It would be interesting to see if changing the dysglycemia cutoff values for each of the risk scores would improve the sensitivity and specificity of the risk scores.

Overall, there were small differences in the performance of the three risk scores in this analysis. CANRISK which was the most sensitive was the least specific, with the inverse being true for FINDRISC. The Saudi-specific score was more balanced, but not as sensitive as CANRISK or as specific as FINDRISC. Given that no risk score clearly outperformed the others, it may be more practical to use the simpler Saudi-specific score, which only has four questions compared to FINDRISC and CANRISK, which have eight and twelve questions, respectively. For screening in more ethnically diverse populations, particularly in gulf countries with a high proportion of expats, CANRISK may be more appropriate since it is the only score that includes ethnicity as a risk factor.

A limitation of this study was the validation was done using cross-sectional data. Additionally, only 49.5% of all SHIS participants completed the lab exam portion of the survey. This limited our analysis to only be able to include participants who had completed the lab portion and who had answered all of the questions included in the risk scores (n=4,611; 42.6%

of all SHIS participants). However, the SHIS survey did offer us a large sample of individuals with HbA1c scores that could be used to externally validate existing risk scores using data specific to the Saudi population. This is the first study to our knowledge that has validated dysglycemia risk scores in Saudi Arabia using data from a nationally representative survey.

Family history of diabetes was only asked to those who positively responded to being previously diagnosed with diabetes. Because of this, we only had family history of diabetes for those who had been diagnosed with diabetes, which would not allow us to do the analysis for FINDRISC or CANDRISK since both risk scores include family history of diabetes. We imputed the values for family history of diabetes for individuals who had not been diagnosed with diabetes. This limited the statistical strength of our analysis. For future surveys, family history of diabetes should be asked to all participants regardless of diabetes status, because it is an important component for many commonly used risk scores.

We had to make some adjustments to CANRISK based on the data collected in SHIS. The SHIS survey only asked about the presence of family history of diabetes, so when we calculated scores using CANRISK we were not able to take into account the additive effect of having multiple family members with diabetes. We also used gestational diabetes as a proxy for macrosomia, which was not collected in SHIS.

Lastly, both FINDRISC and CANRISK included questions on ever being told you had high blood glucose including impaired fasting glucose, impaired glucose tolerance, or gestational diabetes or prediabetes. Both Impaired fasting glucose and impaired glucose tolerance are forms of prediabetes. Since we used CANRISK and FINDRISC to predict dysglycemia, which includes prediabetes and diabetes, there was some overlap in our exposure of being diagnosed

with high blood glucose and our outcome of prediabetes (as part of dysglycemia). The amount of overlap was small as only 2.6% of participants reported being diagnosed with prediabetes.

Implications and Future Directions

Our findings suggest that while there is promise that a rapid, Saudi-specific dysglycemia risk score could be an effective screening tool, there is need to better calibrate existing risk scores if they are to be used in Saudi Arabia. This may include adjusting cutoffs and variables in the risk scores. In order to inform policy more appropriately, there is also a need to collect longitudinal data for the Saudi or greater Arab population and to validate existing and/or develop new risk scores that may be valuable in this population.

More research also needs to be done on the implementation of risk scores in Saudi Arabia and understanding why individuals are not getting diagnosed. It could be because providers are not using risk scores and are not sending patients to receive diagnostic testing. Or it could be that patients are unwilling to get tested. For instance, if providers do not have enough time with patients to use the risk scores, implementing a simpler, faster risk score may be most appropriate. Understanding the barriers in receiving a diagnosis can inform the decision of which risk score should be used, and how it should be implemented.

As diabetes continues to be a growing public health problem for the Kingdom of Saudi Arabia and the Middle East, developing an appropriate, effective screening methods to detect dysglycemia in Saudi Arabia is crucial to provide timely diagnosis, care and prevention of Type 2 diabetes.

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CHAPTER 4: CONCLUSIONS AND RECOMMENDATIONS

The Kingdom of Saudi Arabia has undergone a rapid epidemiological transition over the last few decades as revenue from oil has risen. This rapid shift has left the country with a challenge in controlling, managing, and preventing the growing burden of chronic, non-communicable diseases. As the burden of diabetes grows in the Saudi Arabia, health officials will need to control, treat, and prevent the disease on both a population and individual level. 13.4% of the adult population is estimated to have diabetes, half of which do not even know they have the disease (El Bcheraoui et al., 2014; Zabetian et al., 2013). Effective screening for diabetes and prediabetes will be critical for linking individuals to care for both treatment and prevention.

Most current dysglycemia and diabetes risk scores have been developed using data from high income, developed countries, with the assumption that they can be reasonably applied to other settings. As the Saudi Ministry of Health looks towards standardizing best, evidence-based practices for control and prevention of diabetes, there is a need for country-specific evidence to inform guidelines and decision-making. The development of a Saudi-specific risk score developed by *Memish, et al.* (2015), and the 2012 Saudi Health Interview Survey are positive steps toward this. Our analysis found that the Saudi-specific risk score developed by *Memish, et al.* did not perform much differently from the commonly used Finnish and Canadian risk scores, and had the most balanced sensitivity and specificity of the three scores.

Given there was no risk score that clearly outperformed the others, it may be more practical to use the simpler Saudi-specific risk score, which only has four questions compared to

FINDRISC and CANRISK, which have eight and twelve questions, respectively. For screening in more ethnically diverse populations, particularly in gulf countries with a high proportion of expats, CANRISK may be more appropriate since it is the only risk score that includes ethnicity as a risk factor.

Our findings show there potential to use this rapid risk score, as it has shown promise in our analysis to perform at least as well as the Canadian diabetes risk score, and better than the Finnish diabetes risk score. However, due to its low sensitivities in predicting undiagnosed dysglycemia and diabetes, the Ministry of Health should consider developing a new risk score using nationally representative data, particularly longitudinal data.

Alternatively, the Ministry of Health could further investigate calibrating existing risk scores for the Saudi population. In our analysis, we used predetermined cutoff values for CANRISK and FINDRISC which were set based on studies done in Canada and Finland, respectively. The risk scores may perform better in the Saudi population with a different cutoff value. A sensitivity analysis to determine the optimal cutoff points may be an efficient way to develop an accurate dysglycemia risk score for Saudi Arabia.

Furthermore, more research needs to be done on the implementation of risk scores in Saudi Arabia, and understanding why individuals are not getting diagnosed. It could be because providers are not using risk scores and are not sending patients to receive diagnostic testing. Or it could be that patients are unwilling to get tested. For instance, if providers do not have enough time with patients to use the risk scores, implementing a simpler, faster risk score may be most appropriate. Understanding the barriers in receiving a diagnosis will be crucial to informing the choice of risk score, and how it should be implemented.

TABLES AND FIGURES:

TABLE 1. Criteria for risk scores for screening for dysglycemia using the Saudi Health Interview Survey (SHIS)

Risk factors	Risk scores (Maximum possible points ^a)			Data collected in SHIS
	Saudi-specific dysglycemia score (Memish et al., 2015) (male=16, female=21)	FINDRISC (27)	CANRISK (male=72, female=67)	
Age	30-39 (4 pts) 40-49 (6 pts) 50-59 (10 pts) 60+ (8 pts)	18-44 years (0 pts) 45-54 years (2 pts) 55-64 years (3 pts) 65+ (4 pts)	40-44 years (0 pts) 45-54 years (7 pts) 55-64 years (13 pts) 65-74 years (15 pts)	Self-reported age
Previous history of high blood glucose ^b	History of gestational diabetes only No (0 pts) Yes (5 pts)	No (0 pts) Yes (5 pts)	No (0 pts) Yes (14 pts)	Self-reported diagnosis of gestational diabetes, or pre-diabetes
Waist circumference (cm)	Men < 94 cm (0 pts) ≥ 94 cm (3 pts) Women < 80 cm (0 pts) ≥ 80 cm (3 pts)	Men < 94 cm (0 pts) 94-102 cm (3 pts) >102 cm (4 pts) Women < 80 cm (0 pts) 80-88 cm (3 pts) > 88 cm (4 pts)	Men < 94 cm (0 pts) 94-102 cm (4 pts) >102 cm (6 pts) Women < 80 cm (0 pts) 80-88 cm (4 pts) > 88 cm (6 pts)	Waist circumference measured by interviewer during the household section of survey

History of Hypertension	Self-report diagnosis or systolic pressure \geq 140 mm Hg No (0 pts) Yes (3 pts)	Ever taken medications for high blood pressure on a regular basis No (0 pts) Yes (2 pts)	Defined as self-report diagnosis or as even taken medication for high blood pressure No (0 pts) Yes (4 pts)	Self-reported diagnosis of hypertension and current or previous use of high blood pressure medication
Physically active for more than 30 minutes every day ^c	N/A	Yes ^d (0 pts) No (2 pts)	Yes ^d (0 pts) No (1 pts)	Number of minutes per week of vigorous work activity, moderate work activity, vigorous recreational activity, and moderate recreational activity
Eats vegetables and fruits every day	N/A	Yes (0 pts) No (2 pts)	Yes (0 pts) No (2 pts)	Self-reported number of days per week of fruit and vegetable consumption.
Body Mass Index (BMI) (kg/m ²)	N/A	BMI < 25.0 (0 pts) 25 \leq BMI \leq 29.9 (1 pt) BMI \geq 30 (3 pts)	BMI < 25.0 (0 pts) 25 \leq BMI \leq 29 (4 pts) 30 \leq BMI \leq 34 (9 pts) BMI \geq 35 (14 pts)	Height (cm) and weight (kg) measured by interviewer during the household section of survey
Family history of diabetes mellitus (parents, siblings, or children)	N/A	No (0 pts) Yes (5 pts)	No (0 pts) Mother ^e (2 pts) Father ^e (2 pts) Siblings ^e (2 pts) Children ^e (2 pts)	Self-reported family history of diabetes recorded for participants who responded they had been previously diagnosed with diabetes. Family history of diabetes imputed for the remaining observations.

Gender	N/A	N/A	Male (6 pts) Female (0 pts)	As observed by the interviewer
Macrosomia ^f	N/A	N/A	No (0 pts) Yes (1 point)	Not recorded. Used history of gestational diabetes as a proxy for macrosomia
Race	N/A	N/A	Arab/Saudi (3 pts)	Assumed all participants were Saudi because sampling frame limited to Saudi nationals
What is the highest level of education that you have completed?	N/A	N/A	Some high school or less (5pts) High school completed (1pt) Some college or university (0pts) University degree or higher (0pts)	Highest education level recorded by self-report

Abbreviations: FINDRISC, Finnish Diabetes Risk Score; CANRISK, The Canadian Diabetes Risk Assessment; SHIS, Saudi Health Interview Survey; BMI, body mass index; CM, centimeters; %, percent; PTS, points;

- a. Maximum points that can be earned for the risk score
- b. Includes ever being told you had high blood glucose during a health examination, during an illness, or during pregnancy
- c. Includes physical activity during work, leisure, or regular daily routine.
- d. Defined as ≥ 210 minutes of physical activity per week
- e. For CANRISK, can receive 2 points for each type of family member for a total of 8 points. However, because SHIS did not ask about specific family members with history of diabetes, we restricted the number of points that can be earned to 2 points for respondents with a positive response to the presence of family history of diabetes.
- f. Defined as having given birth to a large baby weighing 9 pounds (4.1 kg) or more

TABLE 2. Characteristics^a of SHIS participants that completed HbA1c testing for blood glucose compared to all participants

	Completed HbA1c testing	All SHIS participants
N	4461	10,821
Age, % (SE)		
15-44	66.00 (0.71)	69.90 (0.44)
45-64	24.30 (0.64)	22.01 (0.40)
≥65	9.71 (0.44)	8.09 (0.26)
Sex, % (SE)		
Female	52.79 (0.75)	51.06 (0.48)
Male	47.21 (0.75)	48.94 (0.48)
BMI, mean (SD)	28.51 (6.58)	28.06 (6.73)
Waist circumference^b in cm, mean (SD)	88.22 (21.77)	85.56 (22.31)
Female	83.23 (21.65)	86.31 (20.68)
Male	87.96 (22.72)	90.33 (22.73)
Eats fruits and vegetables at least 7 days per week^c, % (SE)	51.06 (0.75)	51.52 (0.48)
Engages in moderate to vigorous physical activity at least 7 days per week^d, % (SE)	9.59 (0.44)	9.58 (0.28)
Previous diagnosis of diabetes^e, % (SE)	13.66 (0.51)	11.63 (0.31)
Previous diagnosis of prediabetes^e, % (SE)	2.6 (0.24)	1.79 (0.20)
Previous diagnosis of hypertension^f, % (SE)	11.17 (0.47)	9.57 (0.28)
History of gestational diabetes	1.86 (0.23)	1.84 (0.20)
Education Level, % (SE)		
High school completed	24.77 (0.65)	28.02 (0.43)
University completed/post graduate degree	22.64 (0.63)	23.75 (0.41)

Abbreviations: SHIS, Saudi Health Interview Survey; BMI, body mass index; n, number of participants; SE, standard error; SD, standard deviation; CM, centimeters; %, percent;

- a. All continuous variables were reported with means and standard deviations. All categorical variables were reported with proportions and standard error

TABLE 3. Performance^a of risk scores in identifying dysglycemia among Saudi adults.

	Saudi-specific dysglycemia score (Memish et al., 2015)	FINDRISC	CANRISK
Predicted dysglycemia cutoffs	Score > 8	Score ≥ 12	Score ≥ 21
Sensitivity^b	53.58 (51.36, 55.80)	39.46 (39.43, 39.49)	70.57 (70.54, 70.59)
Specificity^c	75.54 (73.86, 77.21)	82.85 (82.83, 82.86)	55.87 (55.85, 55.89)
PPV^d	62.74 (60.41, 65.07)	63.88 (63.84, 63.92)	55.15 (55.13, 55.17)
NPV^e	67.91 (66.19, 69.64)	64.03 (64.01, 64.04)	71.18 (71.15, 71.20)
Kappa statistic (SE)^f	0.2962 (0.0144)	0.2334 (0.0149)	0.26 (0.0143)

Abbreviations: PPV, positive predictive value; NPV, negative predictive value; FINDRISC, Finnish Diabetes Risk Score; CANRISK, The Canadian Diabetes Risk Assessment; %, percent; SE, standard error

- Data are presented as percentages with 95% confidence intervals based on data from 4461 Saudi adults
- Probability of detecting true dysglycemia (true positives)
- Probability of correctly identifying those without dysglycemia (true negatives)
- Probability of having dysglycemia among those predicted to have dysglycemia.
- Probability of not having dysglycemia among those predicted to not have dysglycemia.
- The Kappa statistic is a measure of agreement between predictions of the risk scores and actual presence or absence of diabetes. n=4461

TABLE 4. Performance^a of risk scores in identifying dysglycemia among Saudi adults without diagnosed dysglycemia (diabetes or prediabetes)

	Saudi-specific dysglycemia score (Memish et al., 2015)	FINDRISC	CANRISK
Predicted dysglycemia cutoff	Score > 8	Score ≥ 12	Score ≥ 21
Sensitivity^b	41.24 (38.52, 43.95)	27.45 (27.41, 27.48)	64.51 (64.47, 64.55)
Specificity^c	75.20 (73.50, 76.90)	82.85 (82.83, 82.86)	53.75 (53.73, 53.77)
PPV^d	45.73 (42.84, 48.63)	44.89 (44.82, 44.96)	41.53 (41.50, 41.55)
NPV^e	71.63 (69.90, 73.36)	69.16 (69.15, 69.18)	74.84 (74.82, 74.86)
Kappa statistic^f (SE)	0.1685 (0.0167)	0.1138 (0.0176)	0.1608 (0.0153)

Abbreviations: PPV, positive predictive value; NPV, negative predictive value; FINDRISC, Finnish Diabetes Risk Score; CANRISK, The Canadian Diabetes Risk Assessment

- a. Data are presented as percentages with 95% confidence intervals based on data from 3806 Saudi adults without diagnosed diabetes or prediabetes
- b. Probability of detecting true dysglycemia (true positives)
- c. Probability of correctly identifying those without dysglycemia (true negatives)
- d. Probability of having dysglycemia among those predicted to have dysglycemia.
- e. Probability of not having dysglycemia among those predicted to not have dysglycemia.
- f. The Kappa statistic is a measure of agreement between predictions of the risk scores and actual presence or absence of diabetes

TABLE 5. Mean scores^a by gender and diabetes status for each risk score

	Saudi-specific dysglycemia score (Memish et al., 2015) (male=16, female=21)^b	FINDRISC^c (27)^b	CANRISK^c (male=72, female=67)^b
All participants^c (n=4461)	6.58 (4.66)	9.17 (4.13)	25.05 (11.73)
Female (n=2355)	6.77 (4.65)	9.80 (4.07)	23.38 (12.14)
Male (n=2106)	6.36 (4.66)	8.48 (4.08)	26.88 (10.90)
Prediabetes^d (n=1099)	7.54 (4.45)	10.13 (4.39)	28.10 (12.64)
Diabetes^e (n=1008)	9.82 (4.09)	11.60 (4.20)	33.81 (11.92)

Abbreviations: FINDRISC, Finnish Diabetes Risk Score; CANRISK, The Canadian Diabetes Risk Assessment; n, number of participants)

- a. Data reported as percentages and standard errors
- b. Maximum possible points for risk score
- c. Includes all participants that completed lab testing portion of survey
- d. Prediabetes defined as self-report diagnosis or HbA1c ≥ 5.7 and < 6.5
- e. Diabetes defined as with self-report diagnosis of HbA1c ≥ 6.5

TABLE 6. Performance^a of risk scores in identifying dysglycemia among Saudi adults by gender

	Saudi-specific dysglycemia score (Memish et al., 2015)		FINDRISC		CANRISK	
	Female	Male	Female	Male	Female	Male
Predicted dysglycemia cutoff	Score > 8	Score > 8	Score ≥ 12	Score ≥ 12	Score ≥ 21	Score ≥ 21
Sensitivity^b	53.54 (50.37, 56.72)	53.62 (50.52, 56.72)	45.12 (45.18, 45.06)	34.08 (34.03, 34.12)	64.52 (57.79, 71.24)	76.32 (76.28, 76.36)
Specificity^c	72.27 (69.93, 74.60)	79.68 (77.31, 82.04)	79.67 (79.64, 79.69)	86.88 (86.86, 86.90)	58.75 (58.72, 58.79)	52.22 (52.18, 52.27)
PPV^d	56.41 (53.17, 59.66)	70.22 (66.97, 73.48)	59.79 (59.72, 59.86)	69.90 (69.81, 69.99)	51.18 (51.14, 51.22)	58.81 (58.77, 58.85)
NPV^e	69.89 (67.54, 72.24)	65.78 (63.24, 68.31)	68.42 (68.39, 68.44)	59.58 (59.55, 59.61)	71.19 (71.15, 71.22)	71.16 (71.11, 71.21)
Kappa statistic (SE)^f	0.2603 (0.0202)	0.3372 (0.0201)	0.2583 (0.0217)	0.2154 (0.0191)	0.2231 (0.0201)	0.2810 (0.0926)

Abbreviations: PPV, positive predictive value; NPV, negative predictive value; FINDRISC, Finnish Diabetes Risk Score; CANRISK, The Canadian Diabetes Risk Assessment; SE, standard error

- Data are presented as percentages with 95% confidence intervals based on data from 4461 Saudi adults without diagnosed diabetes or prediabetes
- Probability of detecting true dysglycemia (true positives)
- Probability of correctly identifying those without dysglycemia (true negatives)
- Probability of having dysglycemia among those predicted to have dysglycemia.
- Probability of not having dysglycemia among those predicted to not have dysglycemia.
- The Kappa statistic is a measure of agreement between predictions of the risk scores and actual presence or absence of diabetes

TABLE 7. Performance^a of risk scores in identifying diabetes among Saudi adults using dysglycemia risk scores.

	Saudi-specific dysglycemia score (Memish et al., 2015)	FINDRISC	CANRISK
Predicted dysglycemia cutoff^b	Score > 8	Score ≥ 12	Score ≥ 21
Sensitivity^b	66.96 (64.06, 69.87)	50.34 (50.29, 50.39)	80.81 (80.78, 80.84)
Specificity^c	71.59 (70.09, 73.09)	79.99 (79.98, 80.00)	51.74 (51.72, 51.75)
PPV^d	40.76 (38.39, 43.13)	42.34 (42.30, 42.38)	32.83 (32.81, 32.85)
NPV^e	88.13 (86.93, 89.33)	84.66 (84.65, 84.66)	90.23 (90.22, 90.24)
Kappa statistic (SE)^f	0.3141 (0.0143)	0.2843 (0.0165)	0.2145 (0.0112)

Abbreviations: PPV, positive predictive value; NPV, negative predictive value; FINDRISC, Finnish Diabetes Risk Score; CANRISK, The Canadian Diabetes Risk Assessment

- Data are presented as percentages with 95% confidence intervals based on data from 4461 Saudi adults without diagnosed diabetes or prediabetes
- Probability of detecting true dysglycemia (true positives)
- Probability of correctly identifying those without dysglycemia (true negatives)
- Probability of having dysglycemia among those predicted to have dysglycemia.
- Probability of not having dysglycemia among those predicted to not have dysglycemia.
- The Kappa statistic is a measure of agreement between predictions of the risk scores and actual presence or absence of diabetes

TABLE 8. Performance^a of risk scores in identifying diabetes among Saudi adults without diagnosed diabetes using dysglycemia risk scores.

	Saudi-specific dysglycemia score (Memish et al., 2015)	FINDRISC	CANRISK
Predicted dysglycemia cutoff	Score > 8	Score ≥ 12	Score ≥ 21
Sensitivity^b	46.97 (41.94, 51.99)	31.32 (31.19, 31.45)	70.96 (70.84, 71.07)
Specificity^c	71.54 (70.02, 73.07)	80.58 (80.57, 80.59)	49.69 (49.67, 49.70)
PPV^d	15.66 (13.54, 17.77)	15.40 (15.36, 15.44)	13.73 (13.72, 13.74)
NPV^e	92.30 (91.28, 93.33)	91.22 (91.22, 91.23)	93.81 (93.80, 93.82)
Kappa statistic (SE)^f	0.0981 (0.0256)	0.0816 (0.0169)	0.0725 (0.0095)

Abbreviations: PPV, positive predictive value; NPV, negative predictive value; FINDRISC, Finnish Diabetes Risk Score; CANRISK, The Canadian Diabetes Risk Assessment

- a. Data are presented as percentages with 95% confidence intervals based on data from 3806 Saudi adults without diagnosed diabetes or prediabetes
- b. Probability of detecting true dysglycemia (true positives)
- c. Probability of correctly identifying those without dysglycemia (true negatives)
- d. Probability of having dysglycemia among those predicted to have dysglycemia.
- e. Probability of not having dysglycemia among those predicted to not have dysglycemia.
- f. The Kappa statistic is a measure of agreement between predictions of the risk scores and actual presence or absence of diabetes