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Saudi Risk Scores for Type 2 Diabetes and Dysglycemia

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# Saudi Risk Scores for Type 2 Diabetes and Dysglycemia

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An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of
Master of Public Health
in Hubert Department of Global Health
2013

# Abstract

Saudi Risk Scores for Type 2 Diabetes and Dysglycemia

By Jennifer Li-chai Chang

**Objective:** To cost-effectively screen for type 2 diabetes in Saudi Arabia, we developed and internally validated risk scoring tools to help identify those with undiagnosed diabetes and dysglycemia.
**Research Design and Methods:** Data from 1,485 non-pregnant Saudi nationals who were ≥ 20 years old and did not have a current diagnosis of diabetes were obtained from urban and rural primary health care centers in 2009. Anthropometric measurements, socio-demographic and lifestyle information, and past medical and family history were obtained through physician-administered interviews. Oral glucose tolerance test data were used to define diabetes (FPG ≥ 126 mg/dL or 2hrPP ≥ 200 mg/dL) and dysglycemia (FPG ≥ 100 mg/dL or 2hrPP ≥ 140mg/dL). Predictive models were developed using data from 1,435 individuals. Multi-variable logistic regression and Receiver-Operating Characteristic curves were used to develop and evaluate two risk scores for each diabetes and dysglycemia. Validation was performed using a hold-out sample of 50 individuals.
**Results:** Both risk scores for undiagnosed diabetes contained age, gestational diabetes, smoking, family history of diabetes, central obesity, and either hypertension or sex with sensitivities ≥ 68% and specificities ≥ 57%. Dysglycemia risk scores contained age, gestational diabetes, hypertension, and either body mass index or waist circumference plus gender with sensitivities ≥ 65% and specificities ≥ 57%. All performed equally well, if not better, in the hold-out sample.
**Conclusions:** Simple non-invasive risk scores from a Saudi adult population can potentially aid in screening for undiagnosed diabetes or dysglycemia and should be further validated in prospective studies.

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ACKNOWLEDGEMENTS

I would like to thank first and foremost my thesis adviser, Mohammed Ali, for his patience, guidance, and encouragement on my thesis. I am also deeply grateful for my collaborators in Saudi Arabia, Dr. Mohammad Al-Hamid, Dr. Omer Abid, and Dr. Ziad Memish, for giving me the privilege to perform the data analysis and to write the manuscript. I would also like to thank Dr. Scott McNabb for starting the collaboration between Emory and the Ministry of Health of Saudi Arabia. Last but not least, I would like to also thank Dr. John Hanfelt and Dr. Paul Weiss for their advice and expertise in statistics.

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# CHAPTER 1: INTRODUCTION

## *Introduction*

It is estimated that diabetes mellitus, also known as diabetes, affected 371 million adults (20-79 years) worldwide in 2012 (Agresti, 2002; Guariguata, 2012). If the total number of people with diabetes was its own country, it would be the third most populous country in the world (Guariguata, 2012). Adults with diabetes comprise 8.3% of the global population, and diabetes is projected to affect 552 million adults by 2030 (Whiting, Guariguata, Weil, & Shaw, 2011).

There are several types of diabetes. The two most common forms of diabetes are Type 1 and Type 2. Type 1 diabetes mellitus (T1DM) is an autoimmune disorder that destroys the beta cells in the pancreas and usually occurs earlier in life (those under the age of 30) (Mantik Lewis, McLean Heitkempter, & Ruff Dirksen, 2004). Since insulin secretion is extremely reduced in T1DM, treatment requires lifelong insulin supplementation (Mantik Lewis et al., 2004). Over 90% of individuals with diabetes have Type 2 diabetes mellitus (T2DM), the only non-autoimmune form of diabetes that is increasing in incidence (Mantik Lewis et al., 2004; Rosenbloom, Joe, Young, & Winter, 1999). T2DM differs from T1DM in that the pancreas continues to secrete insulin. However, insulin production is either insufficient or insulin is poorly utilized by body tissues, resulting in high blood sugar levels, also known as hyperglycemia (Mantik Lewis et al., 2004). T2DM usually occurs later in life and risk increases with age (Goldman & Schafer, 2012). Treatment for T2DM is focused on reducing the incidence of diabetes complications through controlling glucose, blood pressure, and cholesterol levels, and avoiding tobacco, and can be achieved through a combination of lifestyle changes and medications (American Diabetes Association, 2013).

*Prevalence of T2DM in Saudi Arabia*

The International Diabetes Federation (IDF) estimated that diabetes prevalence in the Middle East and North Africa region in 2011 was 12.5% (among 20-79 year olds) and that this will increase to 14.3% in 2030 (Whiting et al., 2011). Saudi Arabia is ranked 6$^{th}$ in the world for highest diabetes prevalence. An estimated 19.6% of people in Saudi Arabia are affected by diabetes and 22.3% are projected to be affected by 2030 (Whiting et al., 2011).

Within the last decade, there has only been one study on T2DM prevalence in Saudi Arabia. This cross-sectional study was limited to one city (Riyadh) and estimated that T2DM occurred among 31.6% of 7-80 year olds. This value is age-adjusted and calculated from 9,149 subjects that were randomly recruited using a cluster sampling strategy from the Biomarker Screening in Riyadh database (n>17,000). When stratified by age groups (18-45 years, 46-60 years, and 61-80 years), the prevalence of T2DM was 12.2%, 46.7%, and 58.2% respectively (Al-Daghri et al., 2011). However, when compared to the prior T2DM prevalence estimate of 7.0% that was obtained from national household surveys between 1992 and 1995, the prevalence of T2DM has increased considerably (Warsy & el-Hazmi, 1999). In either case when comparing the Saudi T2DM prevalence estimates from Al-Dahgri or the IDF, it is strongly evident that the prevalence of T2DM is rising and T2DM is becoming an increasingly common chronic disease in Saudi Arabia.

*Morbidity and Mortality Related to T2DM and the Effects of Early and Comprehensive Risk Factor Control*

T2DM is a disease that involves a progressive decline of beta cell function and insulin sensitivity leading to prolonged episodes of hyperglycemia, known as dysglycemia (Lorenzo et al., 2010). Diabetes occurs at the later end of dysglycemia while prediabetes is used to describe

the period of dysglycemia before diabetes (Buttaro, Trybulski, Bailey, & Sandberg-Cook, 2013). Prolonged periods of hyperglycemia lead to the eventual dysfunction of many organs and emergence of diabetic retinopathy, neuropathy, and nephropathy (Goldman & Schafer, 2012). T2DM increases the risk of vascular diseases and strokes (ischemic, hemorrhagic, and unclassified) up to two times (Emerging Risk Factors Collaboration et al., 2010). In addition, an individual with diabetes without prior myocardial infarction has the same risk of coronary heart disease death compared to an individual without diabetes that has had a prior myocardial infarction (Juutilainen, Lehto, Ronnemaa, Pyorala, & Laakso, 2005). Diabetes increases the risk of all-cause mortality 1.4 – 4.9 times compared to people without diabetes, depending on age and gender (Gu, Cowie, & Harris, 1998). As such, diabetes has major impacts on individuals and their families, and places a heavy burden on health care systems (Valensi et al., 2005).

In the past decade, several studies have shown that early and better blood sugar control reduces one's micro-vascular and long term macro-vascular complications and mortality (Gaede, Lund-Andersen, Parving, & Pedersen, 2008; Holman, Paul, Bethel, Matthews, & Neil, 2008; "Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). UK Prospective Diabetes Study (UKPDS) Group," 1998; Nathan et al., 2005). The United Kingdom Prospective Diabetes Study (UKPDS), to which we attribute many of these findings, is a landmark study that looked at the effects of tight blood sugar control on diabetes related complications. Those assigned to intensive blood sugar control had a median Hemoglobin A1c (HbA1c) of 7.0% over 10 years and were found to have a 25% lower risk of micro-vascular outcomes such as retinopathy requiring photocoagulation, vitreous hemorrhage, or renal failure compared to those in the conventional treatment that had a median HbA1c of 7.9% ("Intensive

blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). UK Prospective Diabetes Study (UKPDS) Group," 1998). A post-trial study done 6-10 years later after the cessation of assigned interventions found those originally in the intensive blood sugar control group had significantly reduced micro-vascular and macro-vascular diabetes complications compared to participants originally in the conventional group, even as HbA1c values of both groups had worsened (Holman et al., 2008). Macro-vascular complications such as myocardial infraction, diabetes-related death, and all-cause mortality were found to be significantly reduced by 15% - 33%, 17-30%-, and 14% -27% respectively, depending on the type of intensive therapy (sulfonylurea and insulin or metformin) originally given (Holman et al., 2008). The sustained health benefit of early intensive blood sugar control has been labeled as the 'legacy effect". Several other studies have also documented the long standing health benefits from early intensive blood sugar control as well (Diabetes Control and Complications Trial [DCCT] and Epidemiology of Diabetes Interventions and Complications [EDIC] study) (Nathan et al., 2005). Other trials targeting very tight glycemic control, like the Action to Control Cardiovascular Risk in Diabetes (ACCORD) and the Action in Diabetes and Vascular Disease: PreterAX and Diamicron Modified Release Controlled Evaluation (ADVANCE) studies showed no effect, perhaps because the characteristics of the populations enrolled at baseline in those trials had a longer mean duration of diabetes and a greater proportion had pre-existing macro-vascular disease (Holman et al., 2008).

Importantly, also, the greatest reductions in overall mortality and diabetes related complications tend to be seen when intensive blood sugar control is coupled with comprehensive risk factor management such as controlling blood pressure, cholesterol, and avoiding smoking.

In the Steno-2 study in Denmark, intensive comprehensive risk factor control for an average of 7.8 years among 160 high-risk patients with pre-existing microalbuminuria was associated with a 53% lower risk of cardiovascular disease (hazard ratio 0.47) and a 58-63% reduction in micro-vascular complications such as retinopathy and nephropathy, compared to usual care (Gaede et al., 2003). At 13.3 years post-intervention, the authors found that those originally in the intensive and comprehensive therapy group had a 57% and 59% risk reduction in cardiovascular deaths and cardiovascular events, respectively, when compared to those with conventional risk factor control (Gaede et al., 2008). Overall, earlier T2DM detection coupled with tight blood sugar control and comprehensive risk factor control is associated with reduced incidence of complications due to T2DM (Buehler et al., 2013; Gaede et al., 2003).

Therefore, it is imperative to diagnose and treat those with T2DM as soon as possible. However, T2DM can be an insidious disease and many are unaware of their condition for up to several years until the onset of complications (Goldman & Schafer, 2012). This phenomenon is common in developed and developing countries of the world. In the U.S., for example, it is estimated that 19-40% of adults with diabetes are undiagnosed (Cheng et al., 2013; Cowie et al., 2010; Cowie et al., 2009). In developing countries undergoing fast economic growth like in China, the number of adults with diabetes that are undiagnosed may even be higher; 60.7% of adults with diabetes in China were undiagnosed according to a national study in 2007-2008 (Yang et al., 2010). As a result, screening is a way to identify those who are currently unaware of their condition.

*Screening*

Screening is an approach that helps identify asymptomatic and/or unaware individuals who are more likely to have a disease, upon whom further diagnostic testing can be performed

(American Diabetes Association, 2003). Screening often involves use of an instrument or tool that can quantify an individual's level of risk of having the disease.

According to the Wilson and Jungner criteria, there are 10 principles that should be satisfied before screening for a disease (Wilson, Jungner, & World Health Organization, 1968). Of these principles, there are three which deserve mention: the disease should be an important health problem with available and acceptable treatment, resources for both diagnosis and treatment must be available, and there should be an acceptable and suitable test during the latent or early symptomatic stage of the disease (Wilson et al., 1968). Examples of screening procedures that are now widely implemented in common practice include those for breast cancer, prostate cancer, and colorectal cancer. For example, the United States Preventative Services Task Force recommends routine screening for colorectal cancer by annual fecal occult blood testing, colonoscopy every 10 years, or sigmoidoscopy every 5 years with fecal occult blood testing every 3 years for those age 50 -75 years old (U.S. Preventive Services Task Force, October 2008). For T2DM, screenings have included both survey instruments and/or biochemical tests (Echouffo-Tcheugui, Ali, Griffin, & Narayan, 2011; World Health Organization, 2003). Currently, guidelines for T2DM do not recommend glucose testing the general population, but rather recommend glucose testing for specific high-risk groups (American Diabetes Association, 2003; World Health Organization, 2003). For example, the American Diabetes Association (ADA) recommends that those who are ≥45 years of age or have a BMI ≥ 25 kg/m2 plus have ≥ 1 risk factor (e.g., previous gestational diabetes, minority race/ethnicity, etc.) are to be screened at 3 years intervals (American Diabetes Association, 2013).

Fasting plasma glucose (FPG) and the oral glucose tolerance test (OGTT) are widely used as screening tests; confusingly, both are also used as diagnostic tests (American Diabetes Association, 2003). FPG requires a single blood draw of serum blood glucose level after at least 8 hours of fasting (American Diabetes Association, 2013). The OGTT entails two blood draws: one FPG and one serum blood glucose level 2 hours after ingesting an anhydrous solution of 75 grams of glucose (2hrPPG) (American Diabetes Association, 2013). FPG is preferred since it is cheaper, easier, faster, convenient, and is more acceptable to the patient, though OGTT remains the gold standard (American Diabetes Association, 2003). However, both screening methods are deemed to be expensive and inconvenient if administered population wide (American Diabetes Association, 2003; Echouffo-Tcheugui et al., 2011). As a result, risk scores that are simple, effective, and non-invasive have been developed to implement targeted glucose testing among high risk individuals.

*Risk Scores*

Risk scores are generally developed using epidemiological data that link exposures (i.e., risk factors like lifestyle, weight, medical history) with outcomes (e.g., diabetes). The use of risk scores as a stepwise screening tool (using 2 tools sequentially as a 2 step process for screening) has been shown to have potential in reducing incident cases of cardiovascular disease (Chamnan, Simmons, Khaw, Wareham, & Griffin, 2010). Risk scores are also considered an efficient approach for detection, rather than testing everyone.

Presently, there is a lack of randomized controlled studies that have displayed the effectiveness of risk scores in reducing mortality or morbidity. Two studies have shown the potential cost effectiveness and reduction of incident T2DM with the utilization of diabetes risk scores in stepwise screening. From the EPIC-Norfolk study, it was estimated that with the

implementation of stepwise screening, less than half of the population will need to undergo further testing compared to population wide testing and will prevent 193 [109-315] versus 224 [130-359] incident cases of diabetes over 3 years (Chamnan, Simmons, Khaw, Wareham, & Griffin, 2012). A modeling study performed in Australia found that using a stepwise screening strategy, a diabetes risk score followed by a FPG or a second diabetes risk score with FPG, had higher cost savings and sensitivity when compared to universal FPG testing (Chen et al., 2011). There was an estimated screening cost of 1080 AUD per case with a diabetes risk score followed by a FPG and 1050 AUD with a diabetes risk score followed by a second diabetes risk score with FPG. Both cost less when compared to the cost of population wide FPG screening (1350 AUD) and the use of a diabetes risk factor score alone (1130 AUD) (Chen et al., 2011). Assuming a 30% relative risk reduction in incident T2DM and 10%, 20%, or 30% of newly diagnosed diabetes becoming non-diabetic following lifestyle intervention, the combined cost of any one of the screening strategies plus lifestyle intervention was less than the cost of population wide screening by FPG and the intervention together (Chen et al., 2011). The authors concluded that the use of a diabetes risk score followed by a second diabetes risk score with a FPG is the least costly and has the highest sensitivity (80.3% [95% CI: 76.6 – 84.1%]) (Chen et al., 2011). In general, there is a growing body of evidence that supports screening for detecting undiagnosed T2DM (Waugh et al., 2007).

Several risk scores have been developed; most are country specific like in Thailand, Finland, Brazil, India, United Kingdom, Oman, and Taiwan (Al-Lawati & Tuomilehto, 2007; Griffin, Little, Hales, Kinmonth, & Wareham, 2000; Keesukphan, Chanprasertyothin, Ongphiphadhanakul, & Puavilai, 2007; Lindstrom & Tuomilehto, 2003; Mohan, Deepa, Deepa, Somannavar, & Datta, 2005; Pires de Sousa et al., 2009; Sun, Tao, & Zhan, 2009). The most

well-known risk score is the Finnish Diabetes Risk Score (FINDRISC). First developed in Finland, FINDRISC is a simple screening tool that encompasses 7 variables (age, BMI, waist circumference, history of treatment for hypertension and hyperglycemia, physical activity, and fruit/vegetable consumption) that predicts the 10 year risk of T2DM among 35-64 year olds (Lindstrom & Tuomilehto, 2003). It has been tested and modified for other populations and is used to predict as well screen for T2DM (Bergmann et al., 2007; Bonaccorsi, Guarducci, Ruffoli, & Lorini, 2012; Garcia-Alcala, Genestier-Tamborero, Hirales-Tamez, Salinas-Palma, & Soto-Vega, 2012; Makrilakis et al., 2011; Tankova, Chakarova, Atanassova, & Dakovska, 2011; Thoopputra, Newby, Schneider, & Li, 2012; Winkler, Hidvegi, Vandorfi, Balogh, & Jermendy, 2013).

Risk scores need to be easy to implement, simple, effective, and their purpose clearly defined. In other words, is the risk score aimed at predicting the risk of T2DM or is it aimed at assisting in finding individuals with undiagnosed diabetes? In addition, risk scores need to be validated in their target populations. Baseline characteristics between populations in which the risk score was developed may be inherently different from the target population.

### *Problem Statement*

Type 2 Diabetes Mellitus (T2DM) is a chronic condition that is defined by insulin insufficiency and/or insulin resistance that can lead to many other chronic conditions and eventual organ dysfunction such as cardiovascular disease and renal failure (Emerging Risk Factors Collaboration et al., 2010; Goldman & Schafer, 2012; Mantik Lewis et al., 2004). It is a condition that requires lifelong changes and has a huge impact on the individual and the family (Valensi et al., 2005). Currently, Saudi Arabia, not unlike the rest of the world, is experiencing

an increased prevalence of T2DM in their population (Whiting, Guariguata, Weil, & Shaw, 2011). Comparable estimates, such as those from the International Diabetes Federation, show that Saudi Arabia has one of the highest diabetes prevalence estimates in the world. Earlier detection and better blood sugar control reduces complications and mortality, but it is challenging to intervene if 19% to 60.7% of the population with diabetes remain undiagnosed (Buehler et al., 2013; Cowie et al., 2010; Cowie et al., 2009; Yang et al., 2010). We can detect those that are currently unaware of their condition with tools or laboratory tests. For T2DM, fasting plasma glucose levels or an oral glucose tolerance test provide good diagnostic tests to confirm T2DM or who are high-risk. Both tests require fasting for at least 8 hours and have been described as inconvenient and expensive. As a result, a simple, efficient, and cost effective screening risk scores are needed that help assess risk and guide practitioners to individuals who should be offered a glucose test.

Numerous risk scores have been developed, largely in Europe. However risk scores need to be developed and validated in their target population. Currently, only one such risk score has been previously developed for Saudi Arabia, but was developed from a weak study design, a small convenience sample of Arabs and non-Arabs from malls and mosques from two cities (Handlos et al., 2013). A diabetes risk score for Saudi Arabia will provide a simple, effective, non-invasive, and cost effective way for healthcare practitioners to identify those who are at risk for T2DM and need to receive diagnostic testing.

## *Purpose Statement*

*Primary:*

- The formulation of a Type 2 Diabetes risk score for Saudi Arabian adults (≥ 20 years) in Saudi Arabia by variable selection and their relative weights.

- The identification of factors that are associated with T2DM in Saudi Arabia and can be targeted to prevent and control diabetes better.

*Secondary:*

- The formulation of a dysglycemia risk score for Saudi Arabian adults (≥ 20 years) in Saudi Arabia by variable selection and their relative weights.
- The identification of factors that are associated with dysglycemia in Saudi Arabia and can be targeted to prevent the onset of diabetes.

### *Significance Statement*

The development of a T2DM risk score will help local healthcare professionals efficiently identify those who are at high risk for T2DM and in need of further diagnostic glucose testing. Detecting T2DM earlier will allow healthcare professionals to intervene and assist patients in the management of their blood sugar and sustain a longer and higher quality of life while reducing their risk of long-term complications, leading to a reduction in the cost burden of the disease. The risk score may also be a more suitable risk score for populations with diabetes phenotypes that are similar to that found in Saudi Arabia. In addition, this research study will add to the scarce body of knowledge concerning factors that are uniquely associated with T2DM in the Middle Eastern region and be able to provide further insight on possible points of intervention.

### *Definition of Terms*

Adults: Persons ≥ 20 years of age.

T2DM: Type 2 Diabetes Mellitus – the non-autoimmune loss of beta cell function and/or insulin sensitivity that is associated with disordered glucose regulation and progresses to fatal and disabling diabetes complications (Mantik Lewis et al., 2004).

Dysglycemia: Encompasses both diabetes and the period of hyperglycemia, prediabetes, which occurs before the development of diabetes (Buttaro et al., 2013).

Screening: Screening is a tool or instrument that identifies asymptomatic and/or unaware individuals who are more likely to have a disease within whom further diagnostic testing can be performed (American Diabetes Association, 2003).

Risk score: A formula that is composed of a combination of weighted lifestyle, physiological, environmental, and/or biochemical risk factors to achieve a number that either signifies the risk of someone developing the disease and/or unaware of having the disease that requires further screening or diagnostic test.

*References*

Agresti, Alan. (2002). *Categorical Data Analysis* (2nd ed.). United States of America: John Wiley & Sons, Inc.

Al-Daghri, N. M., Al-Attas, O. S., Alokail, M. S., Alkharfy, K. M., Yousef, M., Sabico, S. L., & Chrousos, G. P. (2011). Diabetes mellitus type 2 and other chronic non-communicable diseases in the central region, Saudi Arabia (Riyadh cohort 2): a decade of an epidemic. *BMC Med, 9*, 76. doi: 10.1186/1741-7015-9-76

Al-Lawati, J. A., & Tuomilehto, J. (2007). Diabetes risk score in Oman: a tool to identify prevalent type 2 diabetes among Arabs of the Middle East. *Diabetes Res Clin Pract, 77*(3), 438-444. doi: 10.1016/j.diabres.2007.01.013

American Diabetes Association. (2003). Screening for type 2 diabetes. *Diabetes Care, 26 Suppl 1*, S21-24.

American Diabetes Association. (2013). Standards of medical care in diabetes--2013. *Diabetes Care, 36 Suppl 1*, S11-66. doi: 10.2337/dc13-S011

Bergmann, A., Li, J., Wang, L., Schulze, J., Bornstein, S. R., & Schwarz, P. E. (2007). A simplified Finnish diabetes risk score to predict type 2 diabetes risk and disease evolution in a German population. *Horm Metab Res, 39*(9), 677-682. doi: 10.1055/s-2007-985353

Bonaccorsi, G., Guarducci, S., Ruffoli, E., & Lorini, C. (2012). Diabetes screening in primary care: the PRE.DI.CO. study. *Ann Ig, 24*(6), 527-534.

Buehler, A. M., Cavalcanti, A. B., Berwanger, O., Figueiro, M., Laranjeira, L. N., Zazula, A. D., . . . Bordin, S. A. (2013). Effect of tight blood glucose control versus conventional control in patients with type 2 diabetes mellitus: a systematic review with meta-analysis

of randomized controlled trials. *Cardiovasc Ther, 31*(3), 147-160. doi: 10.1111/j.1755-5922.2011.00308.x

Buttaro, Terry Mahan, Trybulski, JoAnn, Bailey, Patricia Polgar, & Sandberg-Cook, Joanne. (2013). *Primary Care: A Collaborative Practice* (4th ed.). USA: Mosby, an imprint of Elsevier Inc.

Chamnan, P., Simmons, R. K., Khaw, K. T., Wareham, N. J., & Griffin, S. J. (2010). Estimating the population impact of screening strategies for identifying and treating people at high risk of cardiovascular disease: modelling study. *BMJ, 340*, c1693. doi: 10.1136/bmj.c1693

Chamnan, P., Simmons, R. K., Khaw, K. T., Wareham, N. J., & Griffin, S. J. (2012). Estimating the potential population impact of stepwise screening strategies for identifying and treating individuals at high risk of Type 2 diabetes: a modelling study. *Diabet Med, 29*(7), 893-904. doi: 10.1111/j.1464-5491.2012.03609.x

Chen, L., Magliano, D. J., Balkau, B., Wolfe, R., Brown, L., Tonkin, A. M., . . . Shaw, J. E. (2011). Maximizing efficiency and cost-effectiveness of Type 2 diabetes screening: the AusDiab study. *Diabet Med, 28*(4), 414-423. doi: 10.1111/j.1464-5491.2010.03188.x

Cheng, Y. J., Imperatore, G., Geiss, L. S., Wang, J., Saydah, S. H., Cowie, C. C., & Gregg, E. W. (2013). Secular changes in the age-specific prevalence of diabetes among U.S. adults: 1988-2010. *Diabetes Care, 36*(9), 2690-2696. doi: 10.2337/dc12-2074

Cowie, C. C., Rust, K. F., Byrd-Holt, D. D., Gregg, E. W., Ford, E. S., Geiss, L. S., . . . Fradkin, J. E. (2010). Prevalence of diabetes and high risk for diabetes using A1C criteria in the U.S. population in 1988-2006. *Diabetes Care, 33*(3), 562-568. doi: 10.2337/dc09-1524

Cowie, C. C., Rust, K. F., Ford, E. S., Eberhardt, M. S., Byrd-Holt, D. D., Li, C., . . . Geiss, L. S. (2009). Full accounting of diabetes and pre-diabetes in the U.S. population in 1988-1994 and 2005-2006. *Diabetes Care, 32*(2), 287-294. doi: 10.2337/dc08-1296

Echouffo-Tcheugui, J. B., Ali, M. K., Griffin, S. J., & Narayan, K. M. (2011). Screening for type 2 diabetes and dysglycemia. *Epidemiol Rev, 33*(1), 63-87. doi: 10.1093/epirev/mxq020

Emerging Risk Factors Collaboration, Sarwar, N., Gao, P., Seshasai, S. R., Gobin, R., Kaptoge, S., . . . Danesh, J. (2010). Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies. *Lancet, 375*(9733), 2215-2222. doi: 10.1016/S0140-6736(10)60484-9

Gaede, P., Lund-Andersen, H., Parving, H. H., & Pedersen, O. (2008). Effect of a multifactorial intervention on mortality in type 2 diabetes. *N Engl J Med, 358*(6), 580-591. doi: 10.1056/NEJMoa0706245

Gaede, P., Vedel, P., Larsen, N., Jensen, G. V., Parving, H. H., & Pedersen, O. (2003). Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes. *N Engl J Med, 348*(5), 383-393. doi: 10.1056/NEJMoa021778

Garcia-Alcala, H., Genestier-Tamborero, C. N., Hirales-Tamez, O., Salinas-Palma, J., & Soto-Vega, E. (2012). Frequency of diabetes, impaired fasting glucose, and glucose intolerance in high-risk groups identified by a FINDRISC survey in Puebla City, Mexico. *Diabetes Metab Syndr Obes, 5*, 403-406. doi: 10.2147/DMSO.S35545

Goldman, Lee, & Schafer, Andrew. (2012). *Goldman's Cecil Medicine* (24th ed.). United States of Ameria: Elsevier.

Griffin, S. J., Little, P. S., Hales, C. N., Kinmonth, A. L., & Wareham, N. J. (2000). Diabetes risk score: towards earlier detection of type 2 diabetes in general practice. *Diabetes Metab Res Rev, 16*(3), 164-171.

Gu, K., Cowie, C. C., & Harris, M. I. (1998). Mortality in adults with and without diabetes in a national cohort of the U.S. population, 1971-1993. *Diabetes Care, 21*(7), 1138-1145.

Guariguata, L. (2012). By the numbers: new estimates from the IDF Diabetes Atlas Update for 2012. *Diabetes Res Clin Pract, 98*(3), 524-525. doi: 10.1016/j.diabres.2012.11.006

Handlos, L. N., Witte, D. R., Almdal, T. P., Nielsen, L. B., Badawi, S. E., Sheikh, A. R., . . . Vistisen, D. (2013). Risk scores for diabetes and impaired glycaemia in the Middle East and North Africa. *Diabet Med, 30*(4), 443-451. doi: 10.1111/dme.12118

Holman, R. R., Paul, S. K., Bethel, M. A., Matthews, D. R., & Neil, H. A. (2008). 10-year follow-up of intensive glucose control in type 2 diabetes. *N Engl J Med, 359*(15), 1577-1589. doi: 10.1056/NEJMoa0806470

Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). UK Prospective Diabetes Study (UKPDS) Group. (1998). *Lancet, 352*(9131), 837-853.

Juutilainen, A., Lehto, S., Ronnemaa, T., Pyorala, K., & Laakso, M. (2005). Type 2 diabetes as a "coronary heart disease equivalent": an 18-year prospective population-based study in Finnish subjects. *Diabetes Care, 28*(12), 2901-2907.

Keesukphan, P., Chanprasertyothin, S., Ongphiphadhanakul, B., & Puavilai, G. (2007). The development and validation of a diabetes risk score for high-risk Thai adults. *J Med Assoc Thai, 90*(1), 149-154.

Lindstrom, J., & Tuomilehto, J. (2003). The diabetes risk score: a practical tool to predict type 2 diabetes risk. *Diabetes Care, 26*(3), 725-731.

Lorenzo, C., Wagenknecht, L. E., D'Agostino, R. B., Jr., Rewers, M. J., Karter, A. J., & Haffner, S. M. (2010). Insulin resistance, beta-cell dysfunction, and conversion to type 2 diabetes in a multiethnic population: the Insulin Resistance Atherosclerosis Study. *Diabetes Care, 33*(1), 67-72. doi: 10.2337/dc09-1115

Makrilakis, K., Liatis, S., Grammatikou, S., Perrea, D., Stathi, C., Tsiligros, P., & Katsilambros, N. (2011). Validation of the Finnish diabetes risk score (FINDRISC) questionnaire for screening for undiagnosed type 2 diabetes, dysglycaemia and the metabolic syndrome in Greece. *Diabetes Metab, 37*(2), 144-151. doi: 10.1016/j.diabet.2010.09.006

Mantik Lewis, Sharon, McLean Heitkempter, Margaret, & Ruff Dirksen, Shannon. (2004). Diabetes Mellitus. In P. Graber O'Brien, J. Foret Giddens & L. Bucher (Eds.), *Medical-Surgical Nursing: Assessment and Management of Clinical Problems* (6 ed., pp. 1268-1302). Canada: Mosby.

Mohan, V., Deepa, R., Deepa, M., Somannavar, S., & Datta, M. (2005). A simplified Indian Diabetes Risk Score for screening for undiagnosed diabetic subjects. *J Assoc Physicians India, 53*, 759-763.

Nathan, D. M., Cleary, P. A., Backlund, J. Y., Genuth, S. M., Lachin, J. M., Orchard, T. J., . . . Complications Study Research, Group. (2005). Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes. *N Engl J Med, 353*(25), 2643-2653. doi: 10.1056/NEJMoa052187

Pires de Sousa, A. G., Pereira, A. C., Marquezine, G. F., Marques do Nascimento-Neto, R., Freitas, S. N., de, C. Nicolato R. L., . . . Krieger, J. E. (2009). Derivation and external

validation of a simple prediction model for the diagnosis of type 2 diabetes mellitus in the Brazilian urban population. *Eur J Epidemiol, 24*(2), 101-109. doi: 10.1007/s10654-009-9314-2

Rosenbloom, A. L., Joe, J. R., Young, R. S., & Winter, W. E. (1999). Emerging epidemic of type 2 diabetes in youth. *Diabetes Care, 22*(2), 345-354.

Sun, F., Tao, Q., & Zhan, S. (2009). An accurate risk score for estimation 5-year risk of type 2 diabetes based on a health screening population in Taiwan. *Diabetes Res Clin Pract, 85*(2), 228-234. doi: 10.1016/j.diabres.2009.05.005

Tankova, T., Chakarova, N., Atanassova, I., & Dakovska, L. (2011). Evaluation of the Finnish Diabetes Risk Score as a screening tool for impaired fasting glucose, impaired glucose tolerance and undetected diabetes. *Diabetes Res Clin Pract, 92*(1), 46-52. doi: 10.1016/j.diabres.2010.12.020

Thoopputra, T., Newby, D., Schneider, J., & Li, S. C. (2012). Survey of diabetes risk assessment tools: concepts, structure and performance. *Diabetes Metab Res Rev, 28*(6), 485-498. doi: 10.1002/dmrr.2296

U.S. Preventive Services Task Force. (October 2008). Screening for Colorectal Cancer: U.S. Preventive Services Task Force Recommendation Statement. Retrieved November 6, 2013, from http://www.uspreventiveservicestaskforce.org/uspstf08/colocancer/colors.htm

Valensi, P., Schwarz, E. H., Hall, M., Felton, A. M., Maldonato, A., & Mathieu, C. (2005). Pre-diabetes essential action: a European perspective. *Diabetes Metab, 31*(6), 606-620.

Warsy, A. S., & el-Hazmi, M. A. (1999). Diabetes mellitus, hypertension and obesity--common multifactorial disorders in Saudis. *East Mediterr Health J, 5*(6), 1236-1242.

Waugh, N., Scotland, G., McNamee, P., Gillett, M., Brennan, A., Goyder, E., . . . John, A. (2007). Screening for type 2 diabetes: literature review and economic modelling. *Health Technol Assess, 11*(17), iii-iv, ix-xi, 1-125.

Whiting, D. R., Guariguata, L., Weil, C., & Shaw, J. (2011). IDF diabetes atlas: global estimates of the prevalence of diabetes for 2011 and 2030. *Diabetes Res Clin Pract, 94*(3), 311-321. doi: 10.1016/j.diabres.2011.10.029

Wilson, J.M.G., Jungner, Gunner, & World Health Organization. (1968). Principles and practice of screening for disease. *Public Health Papers*(34).

Winkler, G., Hidvegi, T., Vandorfi, G., Balogh, S., & Jermendy, G. (2013). Prevalence of undiagnosed abnormal glucose tolerance in adult patients cared for by general practitioners in Hungary. Results of a risk-stratified screening based on FINDRISC questionnaire. *Med Sci Monit, 19*, 67-72.

World Health Organization. (2003). Screening for type 2 diabetes: report of a world health organization and international diabetes federation meeting. Geneva: World Health Organization.

Yang, W., Lu, J., Weng, J., Jia, W., Ji, L., Xiao, J., . . . Metabolic Disorders Study, Group. (2010). Prevalence of diabetes among men and women in China. *N Engl J Med, 362*(12), 1090-1101. doi: 10.1056/NEJMoa0908292

# CHAPTER 2: COMPREHENSIVE REVIEW OF THE LITERATURE

Currently, there is no single set of guidelines regarding who should be tested for diabetes (American Diabetes Association, 2003; World Health Organization, 2003). Diagnostic tests, OGTT and FPG, are too costly to be implemented population wide; therefore, simple and effective screening tools can be used to determine those who require further diagnostic testing (American Diabetes Association, 2003; Echouffo-Tcheugui, Ali, Griffin, & Narayan, 2011). A risk score is a simple risk assessment tool that can help identify those who are likely to have the disease or are at risk of developing diabetes. Use of risk scores for diabetes and prediabetes detection can reduce the cost and inconvenience associated with population wide diagnostic testing and invasive blood testing (American Diabetes Association, 2003; Waugh et al., 2007; World Health Organization, 2003). A risk score is usually comprised of risk factors that have been shown to be associated with diabetes or the development of diabetes. These often include anthropometric measurements, family history, medical history, and lifestyle factors that are each ranked on a whole integer point system. The decision to test further or to re-assess at a later time point is evaluated by calculating the total score in relation to a cut-off score and the associated probable risk for the disease. This process of classifying the individual's risk of disease is how a risk score is used in practice.

The usefulness and performance of a risk score has generally been described in terms of sensitivity, specificity, and receiver-operating characteristic (ROC) curves. Sensitivity is the probability that a subject is classified as having the disease given that he or she actually has the disease (Kleinbaum, Sullivan, & Barker, 2003). It is calculated as: number of people with the disease classified as diseased (true positives) divided by the total number of people classified as diseased regardless if they have the disease or not (true positives plus false positives). Specificity is the probability that a subject is classified as not having the disease given that he or she actually

does not have the disease. Specificity is calculated as the number of people without the disease classified as non-diseased (true negatives) divided by the total number of people classified as non-diseased regardless if they do or do not have the disease (false negatives plus true negatives) (Kleinbaum et al., 2003).

A higher sensitivity means a test is better at classifying those who actually have the disease as diseased and will have a low probability of being classified as non-diseased, a false positive. When sensitivity is graphed against 1- specificity, the resulting line drawn is known as the ROC curve. The area underneath this curve (AUC) represents the test's ability to discriminate a person with the disease from a person without disease (Van Erkel & Pattynama, 1998). An AUC of 0.5 represents the test's inability to discriminate and is the equivalent of being left to chance and is worthless (Van Erkel & Pattynama, 1998). On the other hand, an AUC of 1 represents the test's ability to perfectly accurately discriminate 100% of the time. An AUC value of 0.7 to 0.9 has been roughly determined to mean that a test is moderately accurate (Greiner, Pfeiffer, & Smith, 2000).

Dysglycemia encompasses both prediabetes and diabetes and is either due to impaired fasting glucose (IFG) and/or impaired glucose tolerance (IGT) (Williamson & Narayan, 2009). It is estimated that 5-10% of those with impaired glycemic control later on develop diabetes annually (Cheng, 2005). However very few risk scores have been developed for dysglycemia as most focus on diabetes as their outcome even though there is a growing body of evidence that early intervention during this stage reduces healthcare costs (Ackermann et al., 2006; Waugh et al., 2007). For the purpose of this literature review, risk scores predicting type 2 diabetes will be the main focus and risk scores for dysglycemia will only be covered where applicable.

*Risk Scores*

Risk scores for diabetes have been developed in many countries, at least one from almost every continent, and a large majority of these risk scores originate from Europe/America and Asia (Thoopputra, Newby, Schneider, & Li, 2012). Some studies have employed longitudinal cohort data while others have used cross-sectional study designs to develop their risk scores. The development of one of the most notable risk scores, FINDRISC, shall be presented, followed by a discussion of diabetes risk scores developed in the Middle East. Further details of each of the studies may be found in Table 1.

FINDRISC was first developed in 2003 to identify people with increased risk for T2DM (Lindstrom & Tuomilehto, 2003). The authors used a random sample of 4,746 men and women (aged 25-64 years old) not taking diabetic medications from Finland's National Population Register in 1987. Data covering a follow-up period of 10 years were used. The risk score was then validated in an independent population from health survey data collected in Finland in 1992. FINDRISC was applied at baseline and compared to those with drug treated diabetes during the 5 years of follow up. Logistic regression without considering interaction terms were used to develop the risk score. The authors used bivariate analysis to determine which variables to include in the model, but also included variables that were in accordance with the diabetes literature, even if they were not statistically related to the outcome. In the final model, 7 variables were included: age, BMI, waist circumference, history of taking anti-hypertensives, history of high blood glucose, physical activity, and daily consumption of fruits, berries, or vegetables. This model performed well, as reflected in a final AUC, specificity, and sensitivity of 0.85, 77%, and 78% respectively. Validation with the external cohort also had an AUC of 0.87. Besides developing a risk score that identified people with increased risk of developing T2DM in

the next 10 years, they also found that the risk score performed well in identifying those currently with undiagnosed T2DM.

FINDRISC, though developed from a largely Caucasian population, has been tested and validated in at least 6 other countries (Netherlands, Greece, Mexico, Italy, Hungry, Bulgaria, and Germany) (Bergmann et al., 2007; Bonaccorsi, Guarducci, Ruffoli, & Lorini, 2012; Garcia-Alcala, Genestier-Tamborero, Hirales-Tamez, Salinas-Palma, & Soto-Vega, 2012; Makrilakis et al., 2011; Tankova, Chakarova, Atanassova, & Dakovska, 2011; Thoopputra et al., 2012; Winkler, Hidvegi, Vandorfi, Balogh, & Jermendy, 2013). The risk score was developed with strong methodology: the authors used a random sample from a prospective cohort study, and the objectives matched the study design and were validated in an external cohort. However the authors took an interesting approach in the development of FINDRISC. The authors included variables in the model that were non-significant with the outcome but in accordance with the diabetes literature, used history of hyperglycemia to indirectly account for gestational diabetes, did not consider interaction terms, and defined their outcome as drug treated diabetes.

Only statistically significant variables were in the reduced model: age, BMI, waist circumference, antihypertensive drug therapy, and history of hyperglycemia. In order to emphasize the importance of lifestyle factors in the development of diabetes, the authors also included physical activity and fruit and vegetable consumption. The authors justified their choice by arguing the model slightly increased in predictive power while maintaining a parsimonious model and a simple risk score. Quite cleverly, the authors also indirectly accounted for gestational diabetes. Gestational diabetes is a transient occurrence where hyperglycemia occurs due to increased insulin resistance from placental and counter-regulatory hormones (Buttaro, Trybulski, Bailey, & Sandberg-Cook, 2013). Those with gestational diabetes

are at increased risk of later developing T2DM, and hence an important risk factor to consider (Bellamy, Casas, Hingorani, & Williams, 2009). Interaction terms were not considered during the modeling process and the authors argued it was to keep the risk score simple. Interaction terms are better at accounting for the complicated relationships that variables have with the dependent variable; however, the interpretation and the use of the risk score is consequentially more complicated. Of particular interest, the authors defined their outcome as drug treated diabetes rather than hyperglycemia to define diabetes. Thus, the risk score focuses on those with known diabetes, meaning it underestimates overall risk and under detects the number of people with T2DM.

Regardless, FINDRISC has been applied, validated, and adopted in many other countries. FINDRISC has been used as a model from which countries have been able to develop their own diabetes risk scores. When applied to other countries, FINDRISC has often underperformed as a result of extrinsic and intrinsic factors that play a role in T2DM such as cultural, behavioral, and phenotypic factors. One such example, is the difference in diabetes phenotypes between Asians and Caucasians (Rathmann et al., 2005). In Asians, central obesity has been found to be an important predictor of T2DM, while BMI in Caucasians has been found to be a more important predictor (Hu, 2011). Therefore, it is imperative to at least validate the applicability of a risk score in different populations, especially if a population specific risk score has not been previously developed.

Only one diabetes risk score has been developed in Saudi Arabia to date; and 8 risk scores in total have been developed in the Middle Eastern region. Risk scores developed in the Middle Eastern region will be reviewed here.

*Gulf Countries*

The gulf countries entail Oman, Kuwait, Bahrain, United Arab Emirates, Saudi Arabia, and Qatar. These countries are similar in that they have a common history and have similar political economies and culture. All of these countries have undergone drastic transformations brought upon by large oil industries that have brought with them increased wealth, education, development, and longer life expectancy along with an abundance of fast foods and malls to the region (Alsharekh & Springborg, 2008).

*Oman.*

Oman was the first country among the Gulf Countries to develop and validate a diabetes risk score. In 2007, the authors used a cross-sectional study with a sample size of 4,881 from the 1991 National Diabetes Survey to identify those who are at high risk of having T2DM, defined by a 2hrPPG $\geq$ 200 mg/dL among those that underwent an OGTT (Al-Lawati & Tuomilehto, 2007). Only pregnant women, those aged < 20 years old, and diabetics who showed their diabetic medications to the researchers were excluded. Backward stepwise logistic regression was used, without the consideration of interaction terms to develop a risk score that included 5 categorical variables: age, waist circumference, BMI, family history of diabetes, and hypertension status at the time of the survey. This risk score was found to have an AUC of 0.83 [95% CI: 0.82 -0.84], sensitivity of 78.6% [74.6 -82.1%], and a specificity of 73.4% [72-74.7%]. Using data from a 2001 cross-sectional study for validation, the risk score was found to perform well with an AUC of 0.76 [0.74 - 0.79], sensitivity of 62.8% [54.3-70.6%], and specificity of 78.2% [75.8-80.4%].

Development of the Oman risk score was similar to the process used by FINDRISC, though there were some crucial differences. The authors accounted for gestational diabetes by excluding pregnant women; the outcome was defined by OGTT rather than by treatment of

diabetes; and the risk score was developed from cross-sectional data. The Omani score did not include lifestyle factors, and while FINDRISC only took into account the patient's history of hyperglycemia, the Omani diabetes risk score contained family history of diabetes, thus accounting for the genetic component of T2DM risk. Even though the risk score was developed to identify those who are at high risk of developing or having undiagnosed T2DM, the authors acknowledged that by the nature of their cross-sectional study design, they were unable to predict risk, but were only able to demonstrate associations between their variables and diabetes since it was not clear if their variables were truly antecedent to the development of T2DM. At best, the Omani risk score enables healthcare professionals to identify those who are at risk of having undiagnosed diabetes during screening. It is also interesting to note that the authors chose to categorize variables such as BMI, waist circumference, and age which are continuous in nature. This was also done in the development of the FINDRISC. Categorizing continuous variables may be done for the ease of application and simplicity of applying the risk score (i.e. a score can be assigned if a participant has a BMI or waist circumference above a certain threshold). However, much may be gained by keeping the variables continuous as this more accurately reflects the relationship between variables (Collins, Mallett, Omar, & Yu, 2011).

*Kuwait.*

A risk score was developed to identify individuals at high risk for undiagnosed diabetes in the adult population of Kuwait using the American Diabetes Association's (ADA) definition of diabetes: FPG $\geq$ 126 mg/dL or random plasma glucose $\geq$ 200 mg/dL as the outcome (Al Khalaf et al., 2010). The authors developed the risk score using data from a cross-sectional study that had a multi-stage cluster sampling scheme to gather data from 460 ministry employees. Pregnant women and those previously diagnosed with diabetes were excluded. The

authors used forward stepwise logistic regression to achieve a risk score which included 4 categorical variables: age, waist circumference, antihypertensive(s) use, and presence of a sibling with diabetes with an AUC of 0.82, sensitivity of 87%, and a specificity of 64%. The authors did not provide 95% CIs in the article nor did they validate their model. However, the authors did apply the Omani diabetes risk score to their study population and found it to have better sensitivity (96%) but lower specificity (42%). Diabetes was defined differently between the two risk scores. Oman used OGTT while Kuwait used FPG or a random plasma glucose to define their outcome of diabetes which might account for the difference in performance. However, a cautious interpretation suggests that even among Gulf Countries, differences between populations exist and that the application of diabetes risk scores throughout the whole region would, at the very least, require validation in each target population.

The authors derived their risk score from a small sample size that consisted of government employees. Applicability of the risk score to the wider Kuwaiti adult population is questionable and validation needs to be done. In addition, the authors dichotomized continuous variables, thus further simplifying the risk score. For example, the risk score included a family history of diabetes defined by having an affected sibling versus any affected parent or sibling. Parents, children, and siblings of the individual all have a coefficient of genetic relatedness of 0.50 (share 50% of their genetic information). Accounting for all those with a coefficient of relatedness of 0.50 by being less specific, may increase the sensitivity and specificity of the risk score.

Interestingly enough, waist circumference was the only anthropometric measurement that remained in the risk score, while BMI did not. In contrast, both waist circumference and BMI remained in the Omani risk score and FINDRISC.

*Saudi Arabia and United Arab Emirates.*

Only one diabetes risk score has been developed in Saudi Arabia to identify those with undiagnosed diabetes (Handlos et al., 2013). The authors used a convenience sample in a cross-sectional study design, setting up booths to recruit participants from public areas such as malls and in front of mosques in Jeddah and Riyadh. A total of 2,446 persons aged 30-75 years old were recruited. Pregnant women, those previously diagnosed with diabetes except for those with gestational diabetes, severe disease, and those being treated with corticosteroids were excluded. The diabetes outcome was defined as having a HbA1c $\geq$ 6.5%. The authors used a combination of univariate analysis and stepwise backward elimination to develop a risk score that contained 6 categorical variables: age, gender, BMI, gestational diabetes, ethnicity, and number of siblings with diabetes. This risk score had an AUC of 0.69 [0.65 - 0.73], sensitivity of 74% [67-81%], and a specificity of 52% [49 – 54%]. Validation of the risk score was not done.

The study population contained 86.1% Arabs with 46.4% men. The percentage of participants of Saudi nationality is unknown. In addition, the authors did not disclose how and what proportion of total missing information were recoded. 31% of their observations were incomplete. In order to reduce the number of incomplete observations and to retain observations, the authors recoded missing responses for the use of medications, previous illnesses, or family history of diabetes as "no". As such, the ambiguity and the possible large amount of recoded missing information further decreases the validity of the risk score. Overall, the applicability of this Saudi diabetes risk score is limited due to its weak study design. However, the variables age and family history of diabetes are also found in both the Oman and Kuwait derived risk scores.

Identical study design and methods were used to develop a diabetes risk score for the United Arab Emirates (Handlos et al., 2013). The study sample consisted of 1,987 individuals

from the cities of Sharjah, Dubai, and Abu Dhabi. Here, the risk score contained only four categorical variables: age, BMI, gender, and ethnicity. The AUC was 0.69 [0.65 - 0.73], sensitivity was 73% [66-79%], and specificity was 55% [53-58%]. Again, the same methodological issues exist in this risk score as in the Saudi risk score above. However, differences between the two risk scores can most likely be accounted for by differences in the sample population. The UAE study population consisted of 45.3% Arabs and 70.9% were men.

From the data collected, the authors of the Saudi and UAE diabetes risk scores also developed country specific risk scores for dysglycemia, defined as having diabetes or impaired glycemia according to a HbA1c $\geq$ 6.0%. Saudi Arabia's risk score for dysglycemia contained the same variables as its risk score for diabetes except for male and ethnicity and was found to have an AUC of 0.70 [0.67 – 0.72], sensitivity of 74% [70-78%], and a specificity of 55% [53-57%]. UAE's risk score for dysglycemia contained the same variables as its diabetes risk score and had an AUC of 0.70 [0.67-0.72], sensitivity of 78% [73-82%], and a specificity of 52% [50-55%]. For both dysglycemia risk scores, age was found to be the strongest risk factor, followed by BMI.

In summary, a total of three studies have been published regarding diabetes risk scores in Gulf countries (one in Oman, Saudi Arabia and UAE, and Kuwait) (Al-Lawati & Tuomilehto, 2007; Al Khalaf et al., 2010; Handlos et al., 2013). Two studies utilized complex survey design (Kuwait and Oman) to obtain their sample and only one of the two studies validated its developed risk score (Al-Lawati & Tuomilehto, 2007; Al Khalaf et al., 2010). Out of the three studies, the Omani risk score was developed with the strongest study design since its sampling scheme was the most comprehensive and was the only one validated (Al-Lawati & Tuomilehto,

2007). Common variables that were in all four risk scores were age and an anthropometric measurement (BMI and/or waist circumference).

Unfortunately, the one and only risk score developed in Saudi Arabia was developed using data from a poorly designed study which utilized convenience sampling from urban centers, hence greatly limiting the applicability of the risk score (Handlos et al., 2013). Overall, risk scores in the Gulf countries utilized simple clinical measurements and information that can be easily gathered at outpatient clinics. Other risk scores developed in the Middle East have utilized biochemical measurements as well.

*Others*

*Egypt.*

In Egypt, predictive models for diabetes have been developed and validated, one in 2002 and in 2005 (Tabaei, Engelgau, & Herman, 2005; Tabaei & Herman, 2002). Associative or predictive models are necessary and are done before the development of a risk score. Essentially, a risk score is the application and translation of a predictive or associative model into a form (a tool or instrument) that can be used in practice.

In 2002, investigators in Egypt developed a model to estimate the probability of an individual having previously undiagnosed diabetes by employing a cross-sectional design with a sample of 1,032 Egyptians without a history of diabetes from the Diabetes in Egypt Project (Tabaei & Herman, 2002). Using multiple logistic regression and undiagnosed diabetes (FPG $\geq$126 mg/dL and/or 2hrPPG $\geq$ 200 mg/dL) as the outcome, the authors developed a predictive model that consisted of 5 variables: age, sex, BMI, post prandial time (number of hours since last food or drink), and random plasma glucose. This model performed as follows: AUC of 0.88, sensitivity 65%, and specificity of 96%. 95% confidence intervals were not reported. The

authors also validated their model in an external cross-sectional sample that consisted of 1,065 Americans in Massachusetts, Rhode Island, and North Carolina. Surprisingly, the model was found to perform equivalently with a sensitivity of 62% and specificity of 96%. The authors did not provide an AUC.

The authors' decision to include a random capillary blood glucose and the number of hours since last food or drink in the model was to control for the variability in blood sugar levels due to using a random capillary blood glucose test to measure blood glucose. The authors argued it was more sensitive and specific than using a set plasma glucose cut-off value to predict previously undiagnosed diabetes and even performed well in a mixed ethnic population. In addition, the authors did not dichotomize continuous variables adding strength to their model. Also random capillary blood glucose testing is easy, simple, and inexpensive to obtain with handheld glucometers in the clinic without requiring a laboratory or the participant/patient to be fasted. The addition of a biochemical measurement to the model, at least a capillary blood glucose, did not seem to increase the burden to the staff nor the patient.

In 2005, the authors Tabaei, Engelgau, and Herman developed another predictive equation using logistic regression to estimate the probability of having undiagnosed dysglycemia in Egypt, using a study design similar to the study performed in 2002 (Tabaei et al., 2005). The authors defined dysglycemia as having abnormal blood sugar (encompassing both T2DM and impaired glucose tolerance). The authors recruited 1,032 Egyptians without a history of diabetes from the Diabetes in Egypt Project. Using a combination of anthropometric and biochemical measurements with the outcome, dysglycemia, defined as fasting glucose $\geq$ 6.1 mmol/L and /or 2hrPPG $\geq$ 7.8 mmol/L, 7 variables remained in the model after using bivariate analysis and stepwise selection. The 7 variables were age, sex, BMI, post prandial time, systolic blood

pressure, HDL, and random capillary plasma glucose. All continuous variables were kept continuous. In order to validate their model, the authors randomly divided their sample in half: one half to derive their model and the other half to cross validate. The authors found that their model had a sensitivity, specificity, and AUC of 55%, 90%, and 0.82 respectively. In cross validation, the equation had a sensitivity of 53% and a specificity of 89%.

In both studies, 2002 and 2005, the authors found that their predictive models for diabetes and dysglycemia performed better in identifying those with undiagnosed diabetes or dysglycemia when compared to a random capillary plasma glucose cut-off value. However, the authors did not validate their predictive equation for dysglycemia in an external cohort. Cross validation does increase the equation's validity but does not add much to its generalizability since the equation is validated in the same sample from which the equation was derived from – in other words, splitting the sample randomly likely results in the validation population showing a high resemblance to the model derivation population. The predictive equation for dysglycemia was found to be less sensitive and specific compared to the author's predictive equation for undiagnosed diabetes which may be due to a broader range of overlap in blood glucose values among normal individuals and individuals with dysglycemia or a decreased sensitivity from blood glucose testing to detect dysglycemia (Tabaei et al., 2005). In addition, the inclusion of biochemically-measured high density lipoprotein (HDL) may limit the use for an under resourced outpatient clinic as it requires laboratory testing and is probably associated with reduced patient acceptability as a venous sample is needed.

*Iran and Turkey.*

Two studies, one each from Iran and Turkey, looked specifically at the usability of specific biochemical measurements in a diabetes risk score to predict the development of T2DM

(Bozorgmanesh, Hadaegh, Ghaffari, Harati, & Azizi, 2011; Onat et al., 2011). The study in Iran looked at the triglyceride-to-high density lipoprotein cholesterol ratio (TG/HDL-C) and the study in Turkey at serum C-reactive protein (CRP), an inflammatory marker (Chernecky & Berger, 2008). Both studies had population based cohorts that were followed for more than 5 years with a sample size of 3,242 and 2,261, respectively.

The study in Iran utilized forward stepwise multivariate logistic regression for T2DM to develop a reduced model from a full model that included various combinations of anthropometric and biochemical measurements (Bozorgmanesh et al., 2011). At the end, the authors chose a final model that contained 5 variables: systolic blood pressure, family history of diabetes, waist-to-height ratio (WHtR), TG/HDL-C, and fasting plasma glucose levels. The subsequent risk score was found to have a sensitivity of 75%, specificity of 77%, and an AUC of 0.83. The model was not validated, but did perform better than a model that only contained anthropometric measurements (AUC: 0.83 versus 0.75).

Cox proportional hazards models were used to develop an equation that predicted the 8 year risk of T2DM in Turkish adults (Onat et al., 2011). The authors examined for factors related to incident T2DM as defined by FPG $\geq$ 126 mg/dL, 2hrPPG > 200 mg/dL, or the use of diabetes medications. Backwards selection was used to derive several models for men, women, and both. The authors then selected 7 variables to be in the risk score while categorizing continuous variables: family history of diabetes, physical activity, age, waist circumference, fasting plasma glucose, CRP, and non-HDL cholesterol. The equation was found to have an AUC of 0.78 in men and 0.77 in women. A comparison with an equation with only anthropometric measurements was not done. Validation was performed by splitting the study

sample into two. The performance of the risk score was not found to be significantly different in either sample or when combined (P = 0.58).

The use of biochemical measurements in a risk score seems to improve the discrimination of a diabetes risk score by 8% as seen in the study in Iran (Bozorgmanesh et al., 2011). However, these benefits are offset by the need for costly and cumbersome blood draws. Cholesterol levels are routinely drawn at annual physical examinations; however CRP is not routinely tested and is ordered only if it is indicated. In addition, these risk scores are only applicable in clinics that have access to a laboratory. In contrast, the addition of a capillary glucose level to the risk score is much more feasible since a portable glucometer can be used and there is minimal patient discomfort.

### *Conclusion*

There are very few diabetes risk scores that have been developed in the Middle East with either an objective to predict the risk of diabetes or the risk of currently having undiagnosed diabetes, and even fewer for dysglycemia. Few risk scores were developed using a longitudinal cohort and were validated. All of them contained at least one anthropometric measurement. The inclusion of lifestyle factors, biochemical measurements, and family measurements varied among the risk scores and is largely dependent on the data that were collected and associations found in those populations. The use of biochemical measurements does seem to improve the sensitivity and specificity of a diabetes risk score, but will be of limited use in settings where access to a laboratory is difficult and patient acceptability to blood draws are low.

The only diabetes risk score developed for Saudi Arabia is based on a small convenient cross-sectional sample comprised of mixed Arab and non-Arab participants (Handlos et al., 2013). Therefore, a study with a larger sample size made up of a more homogenous sample that

more closely represents the Saudi population is needed to develop a simple and effective diabetes risk score that best aligns with the phenotype of the Saudi Arabian population. In this report, we used data from a cross-sectional study that were collected using a stratified 2-stage cluster sampling design. Our analyses are aimed at developing a simple and effective diabetes risk score to identify those currently with undiagnosed diabetes and to develop a second risk score for dysglycemia to improve screening in a population with a high T2DM disease burden. The results of this study will provide more insights regarding the factors that are uniquely associated with diabetes in the Saudi Arabian population, the Gulf region, and Middle Eastern region at large. These findings will have implications for clinical practice and for developing public health programs to address the growing burdens of diabetes in Saudi Arabia.

**TABLE 1: SUMMARY OF THE LITERATURE ON DIABETES AND DYSGLYCEMIA RISK SCORES IN THE MIDDLE EAST**

| Article | Objective | Sample Size | Study design | Eligibility and Sampling | Risk Score Variables | Defined Outcome | Data Analysis | Performance | Validation Details | Validation Results |
|---|---|---|---|---|---|---|---|---|---|---|
| (Lindstrom & Tuomilehto, 2003) | 1˚ : Identify individuals who are at increased risk for DM | 1˚: N: 4,435 (FINRISK Studies, 1987) | 1˚ : Cohort with 10 year follow up | Exclusions: ≤ 34 and those on anti-diabetic drug treatment at time of baseline survey | Categorical: Age, BMI, WC, history of antihypterensives medications, and history of high blood sugar, physical activity, and daily consumption of fruits, berries, or vegetables.<br><br>TOTAL: 7 variables | 1˚: Drug treated diabetes | Logistic regression | 1˚ :<br>AUC: 0.85<br><br>Sens: 78%<br><br>Spec: 77% | 1˚ N: 4,586 from an external cohort with 5 year follow up, 1992 | 1˚:<br>AUC: 0.87<br><br>Sens: 81%<br><br>Spec. 76% |
| | 2˚ : Identify those who had undiagnosed DM | 2˚: N: 2,525 (FINRISK Studies, 1987) | 2˚ : Cross-section | Same as above | Same as above | 2˚ : Diabetes* | Applied above risk score to cross-sectional sample | 2˚ :<br>AUC = 0.80<br><br>Sens: 77% [66-85%]<br><br>Spec: 66% [64-68%] | 2˚ N: 1,976 from a cross-section of external cohort,1992 | 2˚ :<br>AUC: 0.80<br><br>Sens: 76% [67-83%]<br><br>Spec. 68% [66-70%] |
| Middle East | | | | | | | | | | |
| (Al-Lawati & Tuomilehto, 2007) | Identify individuals of Arab origin at high risk of having DM | N: 4881 (National Diabetes Survey, 1991) | Cross-section | Exclusions: Pregnant women, < 20 years old, reported diabetes & brought their anti-diabetic medicines | Categorical: Age, WC, BMI, family history of diabetes, and hypertension status at time of survey.<br><br>TOTAL: 5 variables | Diabetes* | Backwards stepwise logistic regression. | AUC: 0.83 [0.82-0.84]<br><br>Sens: 78.6% [74.6-82.1%]<br><br>Spec: 73.4% [72.0-74.7%] | N: 1,432 with external cross-sectional study of Omani's, 2001. | AUC: 0.76 [0.74-0.79]<br><br>Sens: 62.8% [54.3-70.6%]<br><br>Spec: 78.2% [75.8-80.4%] |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| (Al Khalaf et al., 2010) | Identify individuals at high risk for undiagnosed DM in the Kuwaiti adult population | N: 460 public sector employees (2007) | Cross-section | Exclusions: Pregnant women and those previously diagnosed with diabetes | Categorical: Age, WC, on blood pressure medication, and diabetes in a sibling.<br><br>TOTAL: 4 variables | Diabetes* | Forward stepwise logistic regression. | AUC: 0.82<br><br>Sens: 87%<br><br>Spec: 64% | No | |
| (Tabaei & Herman, 2002) | Assess the likelihood of previously undiagnosed DM in an individual. | N: 1,032 Egyptians (Diabetes in Egypt Project, July 1992 - October 1993) | Cross-section | Exclusion: History of diabetes | Categorical: Sex<br><br>Continuous: Age, BMI, and capillary plasma glucose, and postprandial time.<br><br>TOTAL: 5 variables | Diabetes* | Multiple logistic regression.** | AUC: 0.88<br><br>Sens: 65%<br><br>Spec: 96% | N: 1065 with external cross-section of Americans in 3 states (Sept. 1995 and July 1998). | Sens: 62%<br><br>Spec: 96% |
| (Tabaei, Engelgau, & Herman, 2005) | Likelihood of dysglycemia | N: 516 Egyptians (Diabetes in Egypt Project, July 1992 - October 1993) | Cross-section | Exclusion: History of diabetes | Categorical: Sex<br><br>Continuous: Age, BMI, systolic blood pressure, HDL, capillary plasma glucose, and postprandial time.<br><br>TOTAL: 7 variables | Dysglycemia (FPG ≥ 6.1 mmol/L and/or 2 hour post ≥ 7.8 mmol/L) | Bivariate and stepwise logistic regression.** | AUC: 0.82<br><br>Sens: 55%<br><br>Spec: 90% | N: 516 by split sample into two equal parts | Sens: 55%<br><br>Spec: 89% |
| (Bozorgmanesh, Hadaegh, Ghaffari, Harati, & Azizi, 2011) | Predict incident DM in an Iranian population | N: 3,242 (Tehran Lipid and Glucose Study) | Population based cohort with 6 year follow up | Exclusion: < 20 years, assigned to the intervention study, has diabetes*, or | Categorical variables: Family history of diabetes, systolic blood pressure, waist to height ratio, | Diabetes* or taking anti-diabetic medication. | Forward stepwise multivariate logistic regression models. | AUC: 0.83 [0.80-0.86]<br><br>Sens: 75%<br><br>Spec. 77% | Internal validation by bootstrap procedure | |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | taking anti-diabetic medication. | triglyceride to HDL ratio, and FPG<br><br>TOTAL: 5 variables | | | | | |
| (Onat et al., 2011) | Estimate the 8 year risk of incident DM | N: 2261 (Turkish Adult Risk Factor Study) | Population based cohort study with 7.6 years follow up | Exclusion: ≤ 28 years, has diabetes*, or taking anti-diabetic medication. | Categorical: Age, family history of diabetes, physical activity, WC, FPG, c reactive protein, non-HDL cholesterol<br><br>TOTAL: 7 variables | Diabetes* or taking anti-diabetic medication. | Cox proportional hazards and backwards regression | AUC:<br>men: 0.78 [0.74-0.83]<br>women: 0.77 [0.73-0.82] | Split sample into two matched samples by sex, age, and BMI | No significant difference between the predictive value among the split sample, overall, or in lowest to highest quintiles (p=0.58). |
| (Handlos et al., 2013) | 1˚: Undiagnosed DM | Saudi:<br>N: 2,446 (Nov. 2010-Dec. 2011)<br>UAE:<br>N: 1,987 (Nov. 2010-Dec. 2011) | Convenience cross-section | Exclusions: History of diabetes (excluding GDM), pregnant women, severe illness or mental impairments, or treated with systemic steroids.<br><br>Inclusions: 30-75 years old | 1˚: UAE: Age, BMI, male, ethnicity Saudi: Age, BMI, male, number of siblings with diabetes, GDM, ethnicity | 1˚: Undiagnosed diabetes* | Backwards stepwise logistic regression. | 1˚:<br>UAE:<br>AUC: 0.69 [0.65-0.73]<br><br>Sens: 73% [66-79%]<br><br>Spec. 55% [53-58%]<br><br>Saudi:<br>AUC: 0.69 [0.65 - 0.73]<br><br>Sens: 74% [67-81%]<br><br>Spec: 52% [49-54%] | Internal validation by bootstrap procedure | |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 2˚: Undiagnosed dysglycemia | Same as above | Same as above | Same as above | 2˚ UAE: Age, BMI, male, and ethnicity Saudi: Age, BMI, number of siblings with diabetes, and GDM | 2˚: Undiagnosed dysglycemia (HbA1c ≥ 6.0%) | Same as above | 2˚ UAE: AUC: 0.70 [0.67-0.72]<br><br>Sens: 78% [73-82%]<br><br>Spec: 52% [50-55%]<br><br>Saudi: AUC: 0.70 [0.67-0.72]<br><br>Sens: 74% [70-78%]<br><br>Spec: 55% [53-57%] | Same as above | |

Definitions:
1˚: Primary Objective
2˚: Secondary Objective
N: Sample Size
DM: Type 2 Diabetes
BMI: Body Mass Index
WC: Waist Circumference
GDM: Gestational Diabetes
HDL: High-Density Lipoprotein
AUC [95% CI]: Area Under the Curve
Sens [95% CI]: Sensitivity
Spec [95%CI]: Specificity

*Diabetes = FPG ≥ 126 mg/dL, 2 hour post or random glucose ≥ 200 mg/dL, or HbA1c ≥ 6.5%
** Considered interaction terms

*References*

Ackermann, R. T., Marrero, D. G., Hicks, K. A., Hoerger, T. J., Sorensen, S., Zhang, P., . . . Herman, W. H. (2006). An evaluation of cost sharing to finance a diet and physical activity intervention to prevent diabetes. *Diabetes Care, 29*(6), 1237-1241. doi: 10.2337/dc05-1709

Al-Lawati, J. A., & Tuomilehto, J. (2007). Diabetes risk score in Oman: a tool to identify prevalent type 2 diabetes among Arabs of the Middle East. *Diabetes Res Clin Pract, 77*(3), 438-444. doi: 10.1016/j.diabres.2007.01.013

Al Khalaf, M. M., Eid, M. M., Najjar, H. A., Alhajry, K. M., Doi, S. A., & Thalib, L. (2010). Screening for diabetes in Kuwait and evaluation of risk scores. *East Mediterr Health J, 16*(7), 725-731.

Alsharekh, Alanoud, & Springborg, Robert. (2008). *Popular Culture and Political Identity in the Arab Gulf States*. Lebanon: London Middle East Institute at SOAS.

American Diabetes Association. (2003). Screening for type 2 diabetes. *Diabetes Care, 26 Suppl 1*, S21-24.

Bellamy, L., Casas, J. P., Hingorani, A. D., & Williams, D. (2009). Type 2 diabetes mellitus after gestational diabetes: a systematic review and meta-analysis. *Lancet, 373*(9677), 1773-1779. doi: 10.1016/S0140-6736(09)60731-5

Bergmann, A., Li, J., Wang, L., Schulze, J., Bornstein, S. R., & Schwarz, P. E. (2007). A simplified Finnish diabetes risk score to predict type 2 diabetes risk and disease evolution in a German population. *Horm Metab Res, 39*(9), 677-682. doi: 10.1055/s-2007-985353

Bonaccorsi, G., Guarducci, S., Ruffoli, E., & Lorini, C. (2012). Diabetes screening in primary care: the PRE.DI.CO. study. *Ann Ig, 24*(6), 527-534.

Bozorgmanesh, M., Hadaegh, F., Ghaffari, S., Harati, H., & Azizi, F. (2011). A simple risk score effectively predicted type 2 diabetes in Iranian adult population: population-based cohort study. *Eur J Public Health, 21*(5), 554-559. doi: 10.1093/eurpub/ckq074

Buttaro, Terry Mahan, Trybulski, JoAnn, Bailey, Patricia Polgar, & Sandberg-Cook, Joanne. (2013). *Primary Care: A Collaborative Practice* (4th ed.). USA: Mosby, an imprint of Elsevier Inc.

Cheng, D. (2005). Prevalence, predisposition and prevention of type II diabetes. *Nutr Metab (Lond), 2*, 29. doi: 10.1186/1743-7075-2-29

Chernecky, Cynthia C., & Berger, Barbara J. (2008). *Laboratory Tests and Diagnostic Procedures* (5th ed.). USA: Saunders, an imprint of Elsevier Inc.

Collins, G. S., Mallett, S., Omar, O., & Yu, L. M. (2011). Developing risk prediction models for type 2 diabetes: a systematic review of methodology and reporting. *BMC Med, 9*, 103. doi: 10.1186/1741-7015-9-103

Echouffo-Tcheugui, J. B., Ali, M. K., Griffin, S. J., & Narayan, K. M. (2011). Screening for type 2 diabetes and dysglycemia. *Epidemiol Rev, 33*(1), 63-87. doi: 10.1093/epirev/mxq020

Garcia-Alcala, H., Genestier-Tamborero, C. N., Hirales-Tamez, O., Salinas-Palma, J., & Soto-Vega, E. (2012). Frequency of diabetes, impaired fasting glucose, and glucose intolerance in high-risk groups identified by a FINDRISC survey in Puebla City, Mexico. *Diabetes Metab Syndr Obes, 5*, 403-406. doi: 10.2147/DMSO.S35545

Greiner, M., Pfeiffer, D., & Smith, R. D. (2000). Principles and practical application of the receiver-operating characteristic analysis for diagnostic tests. *Prev Vet Med, 45*(1-2), 23-41.

Handlos, L. N., Witte, D. R., Almdal, T. P., Nielsen, L. B., Badawi, S. E., Sheikh, A. R., . . . Vistisen, D. (2013). Risk scores for diabetes and impaired glycaemia in the Middle East and North Africa. *Diabet Med, 30*(4), 443-451. doi: 10.1111/dme.12118

Hu, F. B. (2011). Globalization of diabetes: the role of diet, lifestyle, and genes. *Diabetes Care, 34*(6), 1249-1257. doi: 10.2337/dc11-0442

Kleinbaum, David G., Sullivan, Kevin M., & Barker, Nancy D. (2003). *ActivEpi Companion Textbook: A Supplement for Use with the ActiveEpi CD-ROM*. USA: Springer-Verlag NewYork, Inc.

Lindstrom, J., & Tuomilehto, J. (2003). The diabetes risk score: a practical tool to predict type 2 diabetes risk. *Diabetes Care, 26*(3), 725-731.

Makrilakis, K., Liatis, S., Grammatikou, S., Perrea, D., Stathi, C., Tsiligros, P., & Katsilambros, N. (2011). Validation of the Finnish diabetes risk score (FINDRISC) questionnaire for screening for undiagnosed type 2 diabetes, dysglycaemia and the metabolic syndrome in Greece. *Diabetes Metab, 37*(2), 144-151. doi: 10.1016/j.diabet.2010.09.006

Onat, A., Can, G., Yuksel, H., Ayhan, E., Dogan, Y., & Hergenc, G. (2011). An algorithm to predict risk of type 2 diabetes in Turkish adults: contribution of C-reactive protein. *J Endocrinol Invest, 34*(8), 580-586. doi: 10.3275/7323

Rathmann, W., Martin, S., Haastert, B., Icks, A., Holle, R., Lowel, H., . . . Group, Kora Study. (2005). Performance of screening questionnaires and risk scores for undiagnosed diabetes: the KORA Survey 2000. *Arch Intern Med, 165*(4), 436-441. doi: 10.1001/archinte.165.4.436

Tabaei, B. P., Engelgau, M. M., & Herman, W. H. (2005). A multivariate logistic regression equation to screen for dysglycaemia: development and validation. *Diabet Med, 22*(5), 599-605. doi: 10.1111/j.1464-5491.2005.01467.x

Tabaei, B. P., & Herman, W. H. (2002). A multivariate logistic regression equation to screen for diabetes: development and validation. *Diabetes Care, 25*(11), 1999-2003.

Tankova, T., Chakarova, N., Atanassova, I., & Dakovska, L. (2011). Evaluation of the Finnish Diabetes Risk Score as a screening tool for impaired fasting glucose, impaired glucose tolerance and undetected diabetes. *Diabetes Res Clin Pract, 92*(1), 46-52. doi: 10.1016/j.diabres.2010.12.020

Thoopputra, T., Newby, D., Schneider, J., & Li, S. C. (2012). Survey of diabetes risk assessment tools: concepts, structure and performance. *Diabetes Metab Res Rev, 28*(6), 485-498. doi: 10.1002/dmrr.2296

Van Erkel, A. R., & Pattynama, P. M. (1998). Receiver operating characteristic (ROC) analysis: basic principles and applications in radiology. *Eur J Radiol, 27*(2), 88-94.

Waugh, N., Scotland, G., McNamee, P., Gillett, M., Brennan, A., Goyder, E., . . . John, A. (2007). Screening for type 2 diabetes: literature review and economic modelling. *Health Technol Assess, 11*(17), iii-iv, ix-xi, 1-125.

Williamson, D. F., & Narayan, K. M. (2009). Identification of persons with dysglycemia: terminology and practical significance. *Prim Care Diabetes, 3*(4), 211-217. doi: 10.1016/j.pcd.2009.08.006

Winkler, G., Hidvegi, T., Vandorfi, G., Balogh, S., & Jermendy, G. (2013). Prevalence of undiagnosed abnormal glucose tolerance in adult patients cared for by general

practitioners in Hungary. Results of a risk-stratified screening based on FINDRISC questionnaire. *Med Sci Monit, 19,* 67-72.

World Health Organization. (2003). Screening for type 2 diabetes: report of a world health organization and international diabetes federation meeting. Geneva: World Health Organization.

# CHAPTER 3: MANUSCRIPT

In preparation for submission to Diabetes Care

November 22, 2013

# Saudi Risk Scores for Type 2 Diabetes and Dysglycemia

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Word count: 3,349
Tables and Figures: 4

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*Abstract*

**Objective:** To cost-effectively screen for type 2 diabetes in Saudi Arabia, we developed and internally validated risk scoring tools to help identify those with undiagnosed diabetes and dysglycemia.

**Research Design and Methods:** Data from 1,485 non-pregnant Saudi nationals who were ≥ 20 years old and did not have a current diagnosis of diabetes were obtained from urban and rural primary health care centers in 2009. Anthropometric measurements, socio-demographic and lifestyle information, and past medical and family history were obtained through physician-administered interviews. Oral glucose tolerance test data were used to define diabetes (FPG ≥ 126 mg/dL or 2hrPP ≥ 200 mg/dL) and dysglycemia (FPG ≥ 100 mg/dL or 2hrPP ≥ 140mg/dL). Predictive models were developed using data from 1,435 individuals. Multi-variable logistic regression and Receiver-Operating Characteristic curves were used to develop and evaluate two risk scores for each diabetes and dysglycemia. Validation was performed using a hold-out sample of 50 individuals.

**Results:** Both risk scores for undiagnosed diabetes contained age, gestational diabetes, smoking, family history of diabetes, central obesity, and either hypertension or sex with sensitivities ≥ 68% and specificities ≥ 57%. Dysglycemia risk scores contained age, gestational diabetes, hypertension, and either body mass index or waist circumference plus gender with sensitivities ≥ 65% and specificities ≥ 57%. All performed equally well, if not better, in the hold-out sample.

**Conclusions:** Simple non-invasive risk scores from a Saudi adult population can potentially aid in screening for undiagnosed diabetes or dysglycemia and should be further validated in prospective studies.

## *Introduction*

It is estimated that diabetes affected 371 million adults (20-79 years) worldwide in 2012 (International Diabetes Federation, 2012). Over 90% of diabetes cases are type 2 diabetes mellitus (T2DM) (Mantik Lewis, McLean Heitkempter, & Ruff Dirksen, 2004). Saudi Arabia has the 6$^{th}$ highest diabetes prevalence (19.6%) worldwide and is projected to increase to 22.3% by 2030 (Whiting, Guariguata, Weil, & Shaw, 2011). T2DM is a progressive disease which leads to organ dysfunction and in particular, the emergence of retinopathy, neuropathy, and nephropathy (Goldman & Schafer, 2012). T2DM increases the risk of stroke, heart disease, and all-cause mortality by 1.4-4.5 times (Emerging Risk Factors Collaboration et al., 2010; Gu, Cowie, & Harris, 1998; Singh et al., 2013).

Several studies have shown that early glycemic control reduces one's risk for micro- and long-term macro-vascular complications and mortality in people with diabetes ("Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). UK Prospective Diabetes Study (UKPDS) Group," 1998; Gaede, Lund-Andersen, Parving, & Pedersen, 2008; Holman, Paul, Bethel, Matthews, & Neil, 2008; "Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). UK Prospective Diabetes Study (UKPDS) Group," 1998). However, T2DM is an insidious disease and half of those with diabetes worldwide remain unaware until symptoms or complications develop (Goldman & Schafer, 2012; International Diabetes Federation, 2012). In the U.S., 32% of adults with diabetes remain undiagnosed, and this proportion has been noted to be as high as 60.7% in developing countries like China (Cheng et al., 2013; Yang et al., 2010). Dysglycemia, the inadequate regulation of blood glucose levels, refers to both prediabetes (the precursor phase

before diabetes) and T2DM (Buttaro, Trybulski, Bailey, & Sandberg-Cook, 2013). Those with prediabetes have 5-10 times the annual risk of developing diabetes compared to someone with normal glucose levels and tolerance (Gerstein et al., 2007). However, robust evidence has shown that lifestyle interventions can slow the progression from prediabetes to diabetes. Research trials show that intensive lifestyle modification can reduce diabetes incidence by around 60% with lasting reductions of 34 to 43% lower cumulative incidence over a period of 7 to 14 years follow-up (Diabetes Prevention Program Research et al., 2009; Knowler et al., 2002; Li et al., 2008; Lindstrom et al., 2006; Tuomilehto et al., 2001).

Though the imperative is to identify people with prediabetes or T2DM as soon as possible and initiate interventions, current diagnostic tests for T2DM, fasting plasma glucose (FPG) or oral glucose tolerance tests (OGTT), are expensive and inconvenient to be administered population-wide (American Diabetes Association, 2003; Echouffo-Tcheugui, Ali, Griffin, & Narayan, 2011). Screening, via risk scores, is a way to identify asymptomatic and/or unaware individuals who are more likely to have the disease and narrow the pool that should receive further diagnostic testing (American Diabetes Association, 2003). Risk scores for diabetes have shown to be potentially cost-effective, especially through detection of prediabetes and reducing incidence of T2DM through early intervention (Chamnan, Simmons, Khaw, Wareham, & Griffin, 2012; Chen et al., 2011).

A previous effort to develop a T2DM and dysglycemia risk score in Saudi Arabia used data from a small cross-sectional study (comprised of Arab and non-Arabs) from mosques and malls in two cities (Riyadh and Jeddah), reducing the generalizability of these tools (Handlos et al., 2013). We aimed to develop risk scores for undiagnosed T2DM and dysglycemia in Saudi

Arabia using recent nation-wide cross-sectional data to aid in the detection and management of diabetes and dysglycemia.

## *Methods*

### *Study Design*

From May to June of 2009, Saudi nationals were recruited from both rural and urban primary health care centers (PHCCs) by dividing Saudi Arabia into 5 regions (North, East, West, South, and Central). Each region contained 3-5 sub regions, from which 1 rural and 2 urban PHCCs were randomly chosen from one randomly chosen sub region. Non-pregnant participants ≥ 20 years old without a current diagnosis of diabetes were contacted until a target sample of 240 participants (120 males and 120 females with 20 of each gender in each 10-year age strata) from each urban PHCC and 120 participants (60 males and 60 females with 10 of each gender stratified by age in 10 year increments from 20 to 70+ years) from each rural PHCC were recruited. A total of 2,671 participants gave written informed consent and were recruited. This study did not obtain IRB approval since there was no IRB present in KSA at that time. However, measures were taken to ensure that the study was ethical and did not cause undue harm to the study participants.

### *Data Collection*

Participants were either invited to their PHCC or visited by a physician that administered a questionnaire regarding socio-demographic, lifestyle, past medical, and family history, and obtained blood pressure (mmHg) and anthropometric measurements (waist circumference [cm], height [cm], and weight [kg]).

Participants were instructed to fast overnight for at least 8 hours before going to their respective PHCC for an oral glucose tolerance test (fasting plasma glucose or [FPG: mg/dL]

followed by ingestion of a 75 grams anhydrous solution and a 2 hour post-load glucose [2hrPP: mg/dL]).

*Study Variables*

*Outcomes.*

The presence of T2DM was assessed according to the American Diabetes Association (ADA) guidelines: FPG ≥ 126 mg/dL or 2hrPP ≥ 200 mg/dL (American Diabetes Association, 2012). Dysglycemia was defined as either FPG ≥ 100 mg/dL or 2hrPP ≥ 140 mg/dL (American Diabetes Association, 2012).

*Exposures.*

From patients' reports, current age stratum (20-29, 30-39, 40-49, 50-59, 60-69, and 70+), gender, highest education level (illiterate, literate, primary, secondary, and tertiary education or higher), and marital status (single, married [one wife], married [multiple wives], and divorced) were recorded.

Reported lifestyle factors were classified for smoking status (current, former, or never for cigarettes, cigar, pipe, shisha, or guza), average number of days per week engaged in moderate to vigorous activity (0-7 days), and average servings of fruits and/or vegetables consumed per day (1-5 units/day). Missing values were recoded as having an average intake of zero vegetables and/or fruits per day.

Medical history included questions related to the absence or presence of hypertension, gestational diabetes, previous abnormal blood glucose levels, and a family history of diabetes (parents and/or siblings). "Don't know" was coded as missing.

The presence of hypertension was defined by self-report or by an average of 1-3 current blood pressure measurements (if systolic ≥ 140 mmHg or diastolic ≥ 90 mmHg (National Heart

2004). Body Mass Index (BMI) was calculated as: weight (kg) / (height [m])$^2$ and categorized as underweight or normal (< 25.0 kg/m$^2$), overweight (25.0-29.9 kg/m$^2$), and obese (≥ 30.0 kg/m$^2$) (Alberti, Zimmet, & Shaw, 2007). Waist circumference was dichotomized to indicate central obesity if ≥ 80 cm (women) and ≥ 94 cm (men) (Alberti et al., 2007).

*Data Cleaning*

Missing data comprised of incomplete observations, "don't know", and implausible values for the following variables: age (1), education (23), marital status (148), diabetes (232), hypertension (20), gestational diabetes (404), family history of diabetes (248), BMI (22), waist (119), smoking (343), physical activity (28), occupation (114), and numbers of hours slept (24). Implausible values for height (if ≤ 65 cm or ≥ 200 cm), weight (if > 200 kg), BMI (if ≥ 70 kg/m$^2$), waist (≤ 39 cm), average diastolic blood pressure (if < 30 mmHg), and blood sugars (if < 10 mg/dL) were determined by looking at extreme outliers, histograms, as well as physiologic plausibility (Ford, Li, Zhao, & Tsai, 2011).

*Data Analysis*

Data were analyzed using SAS® software version 9.3 (SAS Institute Inc., Cary, NC). Data were treated as a convenience sample that was collected in all regions of the country. This analysis included complete data from 1,485 participants. Fifty observations were randomly chosen for validation, leaving 1,435 observations to construct predictive models for the diabetes and dysglycemia risk scores. Ordinal variables, physical activity and fruits and vegetables intake, were analyzed as continuous variables.

To describe the socio-demographic and clinical characteristics of the population, we reported frequencies and means with standard deviations. We examined whether each exposure variable was associated with the outcome variables (diabetes or dysglycemia) using bivariate

analysis. Exposure variables that were significantly associated ($\alpha < 0.05$) with each outcome or are known to be important based on the diabetes literature were included in the full models for diabetes or dysglycemia.

Collinearity diagnostics were first performed and interactions were not considered in order to keep the model simple and easy to implement. Multivariate logistic regression was used to formulate predictive models by using stepwise (entry $\alpha < 0.10$, stay $\alpha < 0.15$), forwards ($\alpha < 0.10$), and backwards ($\alpha < 0.10$) elimination. The area underneath the curve (AUC) and the Hosmer-Lemeshow (HL) test were used to determine the best candidate models. The AUC represents the test's ability to discriminate a person with the disease from a person without disease (Van Erkel & Pattynama, 1998). An AUC of 0.5 represents the test's inability to discriminate and is the equivalent of being left to chance (Van Erkel & Pattynama, 1998). An AUC value of 0.7 to 0.9 means that a test is moderately accurate (Greiner, Pfeiffer, & Smith, 2000). The HL test is a goodness of fit test that evaluates whether the model fits the data well. A p-value $\geq 0.05$ indicates that the predicted values are not any different from the observed values and the model is an adequate fit while a p-value of $< 0.05$ indicates that the predicted and observed are significantly different (Agresti, 2002).

Examining for the highest AUC values for each predictive model within the main dataset and the 50 observation validation sample led to the selection of two final predictive models for each outcome. Outlier diagnostics were performed on each of the 4 final predictive models. Observations with a standardized pearson residual > l3l were discarded and the analysis rerun.

*Risk score development.*

To develop a risk score comprised of whole integers from the final predictive models, the coefficients of association between each exposure and outcome variable were multiplied by a

whole number. The resulting number was rounded to the closest whole number. For the diabetes risk score, those aged ≥ 70 were given the same weight as those ≥ 60 since the prevalence of diabetes generally increases with older age (Wild, Roglic, Green, Sicree, & King, 2004). For dysglycemia, those aged ≥ 60 were also given the same weight as those ≥ 50.

*Determination of risk score cut-off.*

The equation:

$$e^{\wedge \text{final model}} / (1 + e^{\wedge \text{final model}})$$

was used to calculate the predictive probabilities of each final model and their corresponding sensitivities and specificities by using the Receiver-Operating Characteristic (ROC) curve and the VasserStats clinical calculator 1 (Lowry, 2013). The ROC curve is a plot of sensitivity versus 1- specificity (false positives) (Greiner et al., 2000). An ideal cut-off value was determined by identifying the optimal sensitivity and specificity (a high number of true positives and a low number of false positives) (Greiner et al., 2000). For each model, we chose cut-off values with slightly higher sensitivity than specificity to minimize the number of false negatives.

For internal validation, each final predictive model was compared to the model's performance (AUC, sensitivity, and specificity) in the hold-out sample and the cut-off scores in the model development and validation samples were compared.

## *Results*

Table 2 shows the socio-demographic and anthropometric characteristics of the population. There were more males (62.0%) than females (38.0%); 34.0% were overweight and a further 41.1% were obese, 57.3% had a family history of diabetes, and 78.5% lived in urban areas. An estimated 15.6% of participants had T2DM while 47.5% had dysglycemia.

In Table 3, multi-variable models for each risk score and their corresponding translation to a whole integer scoring system can be found. Overall, each risk score contained an anthropometric measurement, mostly central obesity, along with age, gestational diabetes, and either family history of diabetes or history of hypertension. For all risk scores, increasing age categories were associated with the highest odds of diabetes and dysglycemia followed by gestational diabetes.

*Diabetes*

Both diabetes risk scores had 6 covariates each. Diabetes score 1 (DMscore1) contained age, sex, family history of diabetes, history of gestational diabetes, smoking status, and waist circumference. Diabetes score 2 (DMscore2) contained the same covariates except that hypertension replaced sex. Both scores had fair AUC values of > 0.70 (DMscore1: 0.7067 [0.6716 – 0.7418]; DMscore2: 0.7057 [0.6706 – 0.7407]). ROC curves can be found in Figure 1. The threshold values calculated for each risk score had sensitivities ≥68% and specificities ≥57% (Table 4).

Both risk scores performed well in the validation hold-out sample with minimal decreases in AUC values (DMscore1: 0.6667 [0.5004-0.8329]; DMscore2: 0.6883 [0.5260 - 0.8507]). In addition, optimal thresholds were determined to be similar with both scores achieving higher sensitivities in the validation sample (DMscore1: 88.9% [50.7-99.4%]; DMscore2: 88.9% [50.7 – 99.4%]).

*Dysglycemia*

The two dysglycemia risk scores were comprised of 4 and 5 variables, respectively. The first dysglycemia risk score (DYSscore1) contained: age, history of gestational diabetes, history of hypertension, and BMI. The second dysglycemia risk score (DYSscore2) contained the same

covariates as DYSscore1 except that central obesity replaced BMI and gender was added. The two scores had AUC values ≥ 0.67 (DYSscore1: 0.6701 [0.6425 - 0.6977]; DYSscore2: 0.6731 [0.6455 – 0.7006]). The threshold values calculated had sensitivities ≥65% and specificities ≥ 57%.

When tested in the validation sample, both dysglycemia risk scores had improved AUC values (DYSscore1: 0.7304; DYSscore2: 0.7448), sensitivities, and specificities. Also, sensitivities were ten percentage points higher in the validation sample based on the risk score thresholds calculated.

### *Discussion*

Using data from all five regions of Saudi Arabia, we developed four risk scores to help identify individuals with undiagnosed diabetes or dysglycemia. These risk scores performed as well or better in internal validation testing, and provide an important resource for detection and subsequent prevention or treatment of diabetes and prediabetes in Saudi Arabia.

Our diabetes risk scores, like many other risk scores, were found to contain a combination of sociodemographic variables, anthropometric measurements, and medical history (Al-Lawati & Tuomilehto, 2007; Chen et al., 2010; Lindstrom & Tuomilehto, 2003). Previous diabetes risk scores from the Middle East did not contain smoking, though smoking is included in risk scores from Australia, England, and Wales (Chen et al., 2010; Hippisley-Cox, Coupland, Robson, Sheikh, & Brindle, 2009). Smoking and even secondhand smoke has been found to increase one's risk for T2DM (Lajous et al., 2013; Willi, Bodenmann, Ghali, Faris, & Cornuz, 2007). Central obesity, as defined by waist circumference thresholds, was a stronger predictor for diabetes than BMI (an indicator of overall obesity) which supports current literature that waist circumference is a better indicator for incident diabetes (Bener et al., 2013; Hadaegh, Zabetian,

Harati, & Azizi, 2006; Kodama et al., 2012). In our study, gestational diabetes was found to be the strongest second predictor after age, concurring with the literature that gestational diabetes greatly increases one's risk for T2DM (Bellamy, Casas, Hingorani, & Williams, 2009).

Few have developed risk scores solely for dysglycemia. Instead, diabetes risk scores are frequently used to detect dysglycemia. Only two risk scores for dysglycemia have been developed in the Middle East, one in Egypt and one previously in Saudi Arabia (Handlos et al., 2013; Tabaei, Engelgau, & Herman, 2005). Additionally, one has been developed in the United States (Lee et al., 2013). They all contain age and an anthropometric measurement, but as in our models, lifestyle factors are noticeably absent. This is most likely due to the difficulty in measuring lifestyle factors.

The cut-off values in our risk scores indicating higher risk, had low to moderate sensitivities and specificities (dysglycemia: 64.2 - 68.6%, 56.5 – 58.9%; diabetes: 67.1 – 73.0%. 56.7 – 59.1%) which is not much different from many currently used risk scores. However, they do not perform as well as FINDRISC, which has a high sensitivity (77% [66-85%]) and moderate specificity (66% [65-68%]) for detecting those with undiagnosed diabetes in their study population (Lindstrom & Tuomilehto, 2003). Our dysglycemia risk scores concur with the ADA guidelines for dysglycemia screening. According to the ADA, testing for dysglycemia should be performed for those who are overweight or obese plus one other risk factor (American Diabetes Association, 2013). In those without risk factors, testing should begin at 45 (American Diabetes Association, 2013). For our models, anyone ≥50 years should be tested for dysglycemia and the testing for individuals less than 50 is usually dictated by age and the presence of 1 or 2 other risk factors.

For each T2DM risk score, the cut-off values derived from the analysis and validation dataset were not that different, indicating the reliability of our risk scores (Table 4). However, for dysglycemia, a difference of 3 points was seen in the derived cut-off values for each of our dysglycemia risk scores. The reason for this is not clear. It is possible that our validation sample was too small. Regardless, we recommend that the lower cut-off value be used to maintain a higher sensitivity.

Diabetes is a growing problem and detection of prediabetes and diabetes are prerequisites to achieving lifestyle goals and adequately controlling blood sugars to slow the progression of the disease and prevent the onset of diabetes related complications, respectively ("Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). UK Prospective Diabetes Study (UKPDS) Group," 1998; Lindstrom et al., 2006; Whiting et al., 2011). Diagnostic tests are available and widely accepted (American Diabetes Association, 2003; Chen et al., 2011). As such, T2DM meets the Wilson and Jungner criteria for screening (Wilson, Jungner, & World Health Organization, 1968). However for screening to be successful, there must be linkage from detection to suitable preventive or care services. Without treatment, the disease will further progress. Future studies need to explore the capacity to prevent and treat, as well as linkage post-detection in Saudi Arabia.

Our study is not without its limitations. Though the data were collected in all five regions of the country, we could not account for the complex survey design because the degrees of freedom equaled zero within the first stage of clustering. Hence, these findings offer an improvement on previous efforts to develop a risk score, but may not be generalizable for Saudi Arabia's whole population. Our study was cross-sectional, limiting the strength of the inferences

we can make about diabetes risk. That said, the Cambridge Diabetes Risk Score was developed from cross-sectional data and performed just as well in predicting diabetes risk in a 4.8 year follow-up prospective cohort (Griffin, Little, Hales, Kinmonth, & Wareham, 2000; Rahman, Simmons, Harding, Wareham, & Griffin, 2008). Since no prospective data for Saudi Arabia are available, we were unable to externally validate our results. We retained observations with previous reports of abnormal blood glucose levels because self-reports are not always accurate, and those with dysglycemia can later become normoglycemic (Meigs et al., 2003). We had a large number of incomplete observations with a disproportionate number of male respondents. However, we compared characteristics between our sample of complete observations and the overall study population and did not find major differences. External validation of these risk scores in prospective studies will be important in affirming or revising the scores.

To date, this is the most robust study on diabetes and dysglycemia risk scores that has been conducted in Saudi Arabia. We developed simple risk scores that are easy to implement in PHCCs and can be widely accepted by both health care providers and patients. The risk scores contain simple clinical measurements that do not require invasive testing and patient information that can be easily obtained during a patient interview and examination.

### *Conclusion*

Saudi Arabia is currently facing a diabetes epidemic. With a steady rise in the prevalence of diabetes over the most recent two to three decades, Saudi Arabia will be faced with a juggernaut of chronic disease burdens unless important action is taken. However, with early detection and adequately controlled blood sugars, much diabetes-related morbidity and its burden on the healthcare system can be reduced. These risk scores may offer that impetus to increase detection and subsequent prevention and treatment efforts.

*References*

Agresti, Alan. (2002). *Categorical Data Analysis* (2nd ed.). United States of America: John Wiley & Sons, Inc.

Al-Lawati, J. A., & Tuomilehto, J. (2007). Diabetes risk score in Oman: a tool to identify prevalent type 2 diabetes among Arabs of the Middle East. *Diabetes Res Clin Pract, 77*(3), 438-444. doi: 10.1016/j.diabres.2007.01.013

Alberti, K. G., Zimmet, P., & Shaw, J. (2007). International Diabetes Federation: a consensus on Type 2 diabetes prevention. *Diabet Med, 24*(5), 451-463. doi: 10.1111/j.1464-5491.2007.02157.x

American Diabetes Association. (2003). Screening for type 2 diabetes. *Diabetes Care, 26 Suppl 1*, S21-24.

American Diabetes Association. (2012). Standards of medical care in diabetes--2012. *Diabetes Care, 35 Suppl 1*, S11-63. doi: 10.2337/dc12-s011

American Diabetes Association. (2013). Standards of medical care in diabetes--2013. *Diabetes Care, 36 Suppl 1*, S11-66. doi: 10.2337/dc13-S011

Bellamy, L., Casas, J. P., Hingorani, A. D., & Williams, D. (2009). Type 2 diabetes mellitus after gestational diabetes: a systematic review and meta-analysis. *Lancet, 373*(9677), 1773-1779. doi: 10.1016/S0140-6736(09)60731-5

Bener, A., Yousafzai, M. T., Darwish, S., Al-Hamaq, A. O., Nasralla, E. A., & Abdul-Ghani, M. (2013). Obesity index that better predict metabolic syndrome: body mass index, waist circumference, waist hip ratio, or waist height ratio. *J Obes, 2013*, 269038. doi: 10.1155/2013/269038

Buttaro, Terry Mahan, Trybulski, JoAnn, Bailey, Patricia Polgar, & Sandberg-Cook, Joanne. (2013). *Primary Care: A Collaborative Practice* (4th ed.). USA: Mosby, an imprint of Elsevier Inc.

Chamnan, P., Simmons, R. K., Khaw, K. T., Wareham, N. J., & Griffin, S. J. (2012). Estimating the potential population impact of stepwise screening strategies for identifying and treating individuals at high risk of Type 2 diabetes: a modelling study. *Diabet Med, 29*(7), 893-904. doi: 10.1111/j.1464-5491.2012.03609.x

Chen, L., Magliano, D. J., Balkau, B., Colagiuri, S., Zimmet, P. Z., Tonkin, A. M., . . . Shaw, J. E. (2010). AUSDRISK: an Australian Type 2 Diabetes Risk Assessment Tool based on demographic, lifestyle and simple anthropometric measures. *Med J Aust, 192*(4), 197-202.

Chen, L., Magliano, D. J., Balkau, B., Wolfe, R., Brown, L., Tonkin, A. M., . . . Shaw, J. E. (2011). Maximizing efficiency and cost-effectiveness of Type 2 diabetes screening: the AusDiab study. *Diabet Med, 28*(4), 414-423. doi: 10.1111/j.1464-5491.2010.03188.x

Cheng, Y. J., Imperatore, G., Geiss, L. S., Wang, J., Saydah, S. H., Cowie, C. C., & Gregg, E. W. (2013). Secular changes in the age-specific prevalence of diabetes among U.S. adults: 1988-2010. *Diabetes Care, 36*(9), 2690-2696. doi: 10.2337/dc12-2074

Diabetes Prevention Program Research, Group, Knowler, W. C., Fowler, S. E., Hamman, R. F., Christophi, C. A., Hoffman, H. J., . . . Nathan, D. M. (2009). 10-year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study. *Lancet, 374*(9702), 1677-1686. doi: 10.1016/S0140-6736(09)61457-4

Echouffo-Tcheugui, J. B., Ali, M. K., Griffin, S. J., & Narayan, K. M. (2011). Screening for type 2 diabetes and dysglycemia. *Epidemiol Rev, 33*(1), 63-87. doi: 10.1093/epirev/mxq020

Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). UK Prospective Diabetes Study (UKPDS) Group. (1998). *Lancet, 352*(9131), 854-865.

Emerging Risk Factors Collaboration, Sarwar, N., Gao, P., Seshasai, S. R., Gobin, R., Kaptoge, S., . . . Danesh, J. (2010). Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies. *Lancet, 375*(9733), 2215-2222. doi: 10.1016/S0140-6736(10)60484-9

Ford, E. S., Li, C., Zhao, G., & Tsai, J. (2011). Trends in obesity and abdominal obesity among adults in the United States from 1999-2008. *Int J Obes (Lond), 35*(5), 736-743. doi: 10.1038/ijo.2010.186

Gaede, P., Lund-Andersen, H., Parving, H. H., & Pedersen, O. (2008). Effect of a multifactorial intervention on mortality in type 2 diabetes. *N Engl J Med, 358*(6), 580-591. doi: 10.1056/NEJMoa0706245

Gerstein, H. C., Santaguida, P., Raina, P., Morrison, K. M., Balion, C., Hunt, D., . . . Booker, L. (2007). Annual incidence and relative risk of diabetes in people with various categories of dysglycemia: a systematic overview and meta-analysis of prospective studies. *Diabetes Res Clin Pract, 78*(3), 305-312. doi: 10.1016/j.diabres.2007.05.004

Goldman, Lee, & Schafer, Andrew. (2012). *Goldman's Cecil Medicine* (24th ed.). United States of Ameria: Elsevier.

Greiner, M., Pfeiffer, D., & Smith, R. D. (2000). Principles and practical application of the receiver-operating characteristic analysis for diagnostic tests. *Prev Vet Med, 45*(1-2), 23-41.

Griffin, S. J., Little, P. S., Hales, C. N., Kinmonth, A. L., & Wareham, N. J. (2000). Diabetes risk score: towards earlier detection of type 2 diabetes in general practice. *Diabetes Metab Res Rev, 16*(3), 164-171.

Gu, K., Cowie, C. C., & Harris, M. I. (1998). Mortality in adults with and without diabetes in a national cohort of the U.S. population, 1971-1993. *Diabetes Care, 21*(7), 1138-1145.

Hadaegh, F., Zabetian, A., Harati, H., & Azizi, F. (2006). Waist/height ratio as a better predictor of type 2 diabetes compared to body mass index in Tehranian adult men--a 3.6-year prospective study. *Exp Clin Endocrinol Diabetes, 114*(6), 310-315. doi: 10.1055/s-2006-924123

Handlos, L. N., Witte, D. R., Almdal, T. P., Nielsen, L. B., Badawi, S. E., Sheikh, A. R., . . . Vistisen, D. (2013). Risk scores for diabetes and impaired glycaemia in the Middle East and North Africa. *Diabet Med, 30*(4), 443-451. doi: 10.1111/dme.12118

Hippisley-Cox, J., Coupland, C., Robson, J., Sheikh, A., & Brindle, P. (2009). Predicting risk of type 2 diabetes in England and Wales: prospective derivation and validation of QDScore. *BMJ, 338*, b880. doi: 10.1136/bmj.b880

Holman, R. R., Paul, S. K., Bethel, M. A., Matthews, D. R., & Neil, H. A. (2008). 10-year follow-up of intensive glucose control in type 2 diabetes. *N Engl J Med, 359*(15), 1577-1589. doi: 10.1056/NEJMoa0806470

Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). UK Prospective Diabetes Study (UKPDS) Group. (1998). *Lancet, 352*(9131), 837-853.

International Diabetes Federation. (2012). *IDF Diabetes Atlas Update 2012, 5th edn.* Retrieved from http://www.idf.org/diabetesatlas

Knowler, W. C., Barrett-Connor, E., Fowler, S. E., Hamman, R. F., Lachin, J. M., Walker, E. A., . . . Diabetes Prevention Program Research, Group. (2002). Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med, 346*(6), 393-403. doi: 10.1056/NEJMoa012512

Kodama, S., Horikawa, C., Fujihara, K., Heianza, Y., Hirasawa, R., Yachi, Y., . . . Sone, H. (2012). Comparisons of the strength of associations with future type 2 diabetes risk among anthropometric obesity indicators, including waist-to-height ratio: a meta-analysis. *Am J Epidemiol, 176*(11), 959-969. doi: 10.1093/aje/kws172

Lajous, M., Tondeur, L., Fagherazzi, G., de Lauzon-Guillain, B., Boutron-Ruaualt, M. C., & Clavel-Chapelon, F. (2013). Childhood and adult secondhand smoke and type 2 diabetes in women. *Diabetes Care, 36*(9), 2720-2725. doi: 10.2337/dc12-2173

Lee, J. M., Gebremariam, A., Woolford, S. J., Tarini, B. A., Valerio, M. A., Bashir, S., . . . Gurney, J. G. (2013). A risk score for identifying overweight adolescents with dysglycemia in primary care settings. *J Pediatr Endocrinol Metab, 26*(5-6), 477-488. doi: 10.1515/jpem-2012-0259

Li, G., Zhang, P., Wang, J., Gregg, E. W., Yang, W., Gong, Q., . . . Bennett, P. H. (2008). The long-term effect of lifestyle interventions to prevent diabetes in the China Da Qing Diabetes Prevention Study: a 20-year follow-up study. *Lancet, 371*(9626), 1783-1789. doi: 10.1016/S0140-6736(08)60766-7

Lindstrom, J., Ilanne-Parikka, P., Peltonen, M., Aunola, S., Eriksson, J. G., Hemio, K., . . . Finnish Diabetes Prevention Study, Group. (2006). Sustained reduction in the incidence of type 2 diabetes by lifestyle intervention: follow-up of the Finnish Diabetes Prevention Study. *Lancet, 368*(9548), 1673-1679. doi: 10.1016/S0140-6736(06)69701-8

Lindstrom, J., & Tuomilehto, J. (2003). The diabetes risk score: a practical tool to predict type 2 diabetes risk. *Diabetes Care, 26*(3), 725-731.

Lowry, Richard. (2013). VassarStats- Website for Statistical Computation: Clinical Calculator 1. Retrieved November 14, 2013, from http://vassarstats.net/clin1.html

Mantik Lewis, Sharon, McLean Heitkempter, Margaret, & Ruff Dirksen, Shannon. (2004). Diabetes Mellitus. In P. Graber O'Brien, J. Foret Giddens & L. Bucher (Eds.), *Medical-Surgical Nursing: Assessment and Management of Clinical Problems* (6 ed., pp. 1268-1302). Canada: Mosby.

Meigs, J. B., Muller, D. C., Nathan, D. M., Blake, D. R., Andres, R., & Baltimore Longitudinal Study of, Aging. (2003). The natural history of progression from normal glucose tolerance to type 2 diabetes in the Baltimore Longitudinal Study of Aging. *Diabetes, 52*(6), 1475-1484.

National Heart , Lung, and Blood Institute (US). (2004). The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Bethesda (MD).

Rahman, M., Simmons, R. K., Harding, A. H., Wareham, N. J., & Griffin, S. J. (2008). A simple risk score identifies individuals at high risk of developing Type 2 diabetes: a prospective cohort study. *Fam Pract, 25*(3), 191-196. doi: 10.1093/fampra/cmn024

Singh, G. M., Danaei, G., Farzadfar, F., Stevens, G. A., Woodward, M., Wormser, D., . . . Prospective Studies, Collaboration. (2013). The age-specific quantitative effects of metabolic risk factors on cardiovascular diseases and diabetes: a pooled analysis. *PLoS One, 8*(7), e65174. doi: 10.1371/journal.pone.0065174

Tabaei, B. P., Engelgau, M. M., & Herman, W. H. (2005). A multivariate logistic regression equation to screen for dysglycaemia: development and validation. *Diabet Med, 22*(5), 599-605. doi: 10.1111/j.1464-5491.2005.01467.x

Tuomilehto, J., Lindstrom, J., Eriksson, J. G., Valle, T. T., Hamalainen, H., Ilanne-Parikka, P., . . . Finnish Diabetes Prevention Study, Group. (2001). Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med, 344*(18), 1343-1350. doi: 10.1056/NEJM200105033441801

Van Erkel, A. R., & Pattynama, P. M. (1998). Receiver operating characteristic (ROC) analysis: basic principles and applications in radiology. *Eur J Radiol, 27*(2), 88-94.

Whiting, D. R., Guariguata, L., Weil, C., & Shaw, J. (2011). IDF diabetes atlas: global estimates of the prevalence of diabetes for 2011 and 2030. *Diabetes Res Clin Pract, 94*(3), 311-321. doi: 10.1016/j.diabres.2011.10.029

Wild, S., Roglic, G., Green, A., Sicree, R., & King, H. (2004). Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. *Diabetes Care, 27*(5), 1047-1053.

Willi, C., Bodenmann, P., Ghali, W. A., Faris, P. D., & Cornuz, J. (2007). Active smoking and the risk of type 2 diabetes: a systematic review and meta-analysis. *JAMA, 298*(22), 2654-2664. doi: 10.1001/jama.298.22.2654

Wilson, J.M.G., Jungner, Gunner, & World Health Organization. (1968). Principles and practice of screening for disease. *Public Health Papers*(34).

Yang, W., Lu, J., Weng, J., Jia, W., Ji, L., Xiao, J., . . . Metabolic Disorders Study, Group. (2010). Prevalence of diabetes among men and women in China. *N Engl J Med, 362*(12), 1090-1101. doi: 10.1056/NEJMoa0908292

**TABLE 2: POPULATION DEMOGRAPHICS AND PREVALENCE OF PREDIABETES AND DIABETES WITHIN EACH VARIABLE LEVEL FOR NON-PREGNANT SAUDI ADULTS AGED ≥ 20 YEARS (2009)**

| | Variables | Overall Demographics N = 1485 | Prevalence of Prediabetes N = 475 | Prevalence of Diabetes N = 231 |
|---|---|---|---|---|
| Sociodemographics | Gender | | | |
| | Males: | 62.0% | 30.5% | 13.9% |
| | Females: | 38.0% | 34.4% | 18.3% |
| | Age (years) | | | |
| | 20-29: | 19.3% | 19.9% | 4.6% |
| | 30-39: | 21.5% | 31.7% | 10.0% |
| | 40-49: | 20.7% | 32.9% | 17.9% |
| | 50-59: | 17.0% | 41.7% | 22.2% |
| | 60-69: | 13.2% | 30.1% | 29.1% |
| | 70+: | 8.4% | 41.6% | 14.4% |
| | Occupation | | | |
| | White collar: | 50.0% | 28.0% | 12.5% |
| | Student: | 5.0% | 23.3% | 2.7% |
| | Housewife: | 28.0% | 35.7% | 20.7% |
| | Retired: | 14.8% | 42.0% | 19.6% |
| | Unemployed: | 2.4% | 27.8% | 19.4% |
| | Education | | | |
| | Illiterate: | 20.5% | 35.2% | 22.0% |
| | Literate: | 6.9% | 36.9% | 23.3% |
| | Primary Education: | 12.7% | 39.7% | 20.6% |
| | Secondary Education: | 34.0% | 28.9% | 11.1% |
| | Tertiary Education and Higher: | 25.9% | 28.4% | 11.7% |
| | Marital Status | | | |
| | Single: | 12.6% | 24.1% | 5.9% |
| | Married (one wife): | 75.7% | 33.1% | 16.2% |
| | Married (multiple wives): | 3.2% | 31.3% | 18.8% |
| | Divorced: | 2.4% | 37.1% | 20.0% |
| | Widowed: | 6.1% | 33.0% | 24.2% |
| | Urban | 78.5% | 32.5% | 15.5% |
| | Rural | | 30.1% | 15.7% |
| | Region | | | |
| | Aljouf: | 22.4% | 26.1% | 14.1% |
| | Riyadh: | 25.7% | 39.3% | 14.9% |
| | Eastern Province: | 17.2% | 18.0% | 18.4% |
| | Jazan: | 20.4% | 39.3% | 17.8% |
| | Mecca: | 14.3% | 34.4% | 12.3% |
| Past Medical and Family History | Diagnosed with Diabetes | 15.6% | | |
| | Has/Had Hypertension | 34.8% | 38.3% | 21.5% |
| | None: | | 28.6% | 12.4% |
| | Had Gestational Diabetes | 12.1% | 35.3% | 30.9% |
| | None: | | 34.3% | 16.5% |
| | Has Family History of Diabetes | 57.3% | 30.9% | 18.6% |
| | None: | | 33.4% | 11.5% |
| Anthropometric Measurements | BMI: Mean (SD) | 29.4 (6.4) | 30.2 (6.4) | 31.20 (6.3) |
| | <25: | 24.9% | 27.1% | 9.2% |
| | 25 to <30: | 34.0% | 30.1% | 15.1% |
| | ≥ 30: | 41.1% | 36.5% | 19.8% |
| | Waist (cm): Mean (SD) | 94.8 (15.8) | 96.1 (16.3) | 100.0 (15.8) |
| | Central Obesity* | | | |
| | No: | 31.8% | 26.7% | 8.9% |
| | Yes: | 68.2% | 34.5% | 18.7% |

*Central Obesity: Waist circumference for women ≥80 cm, men ≥ 94cm (Alberti et al., 2007)

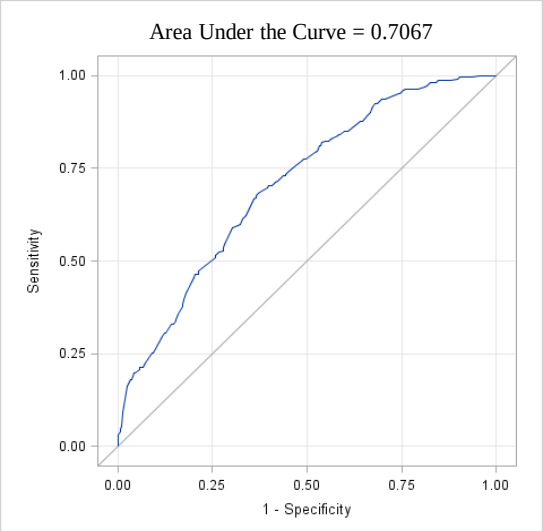
**TABLE 3: TYPE 2 DIABETES MELLITUS AND DYSGLYCEMIA FINAL MODELS AND RISK SCORE DEVELOPMENT FOR NON-PREGNANT SAUDI ADULTS AGED ≥ 20 YEARS, N = 1435 (2009)**

| | OR [95% CI] | β-coef. | Score | | OR [95% CI] | β-coef. | Score |
|---|---|---|---|---|---|---|---|
| **DIABETES** | | | | | | | |
| **MODEL 1** | | | | **MODEL 2** | | | |
| **Intercept** | | -3.9489 | | **Intercept** | | -3.792 | |
| **Age:** | | | | **Age:** | | | |
| **20-29:** | | Reference | 0 | **20-29:** | | Reference | 0 |
| **30-39:** | 1.81 [0.92 – 3.57] | 0.5914 | 2 | **30-39:** | 1.76 [0.89 – 3.48] | 0.5668 | 3 |
| **40-49:** | 3.33 [1.74 – 6.35] | 1.2013 | 5 | **40-49:** | 3.26 [1.71 – 6.24] | 1.1825 | 6 |
| **50-59:** | 5.00 [2.62 – 9.57] | 1.6097 | 6 | **50-59:** | 4.65 [2.41 – 8.97] | 1.5367 | 8 |
| **60-69:** | 7.33 [3.81 – 14.11] | 1.9926 | 8 | **60-69:** | 6.61 [3.39 – 12.89] | 1.8881 | 9 |
| **70+: *** | 2.73 [1.24 -6.03] | 1.0570 | 4 ->8 | **70+: *** | 2.36 [1.05 – 5.32] | 0.8596 | 4->9 |
| **Gender** | | | | **Has/Had HTN** | | | |
| **Male** | | Reference | 0 | **No** | | Reference | 0 |
| **Female** | 1.42 [.97 -2.09] | 0.3526 | 1 | **Yes** | 1.26 [0.92 – 1.74] | 0.234 | 1 |
| **Had GDM** | | | | **Had GDM** | | | |
| **No** | | Reference | 0 | **No** | | Reference | 0 |
| **Yes** | 2.14 [1.17 – 3.91] | 0.7614 | 3 | **Yes** | 2.48 [1.39 -4.43] | 0.9085 | 5 |
| **Smoking** | | | | **Smoking** | | | |
| **Never** | | Reference | 0 | **Never** | | Reference | 0 |
| **Former** | 1.65 [1.03 – 2.63] | 0.5005 | 2 | **Former** | 1.39 [0.91 – 2.11] | 0.3268 | 2 |
| **Current** | 1.75 [1.11 – 2.74] | 0.5587 | 2 | **Current** | 1.47 [0.99 – 2.21] | 0.3882 | 2 |
| **Fam Hx DM** | | | | **Fam Hx DM** | | | |
| **No** | | Reference | 0 | **No** | | Reference | 0 |
| **Yes** | 1.73 [1.26 – 2.37] | 0.5458 | 2 | **Yes** | 1.71 [1.25 – 2.35] | 0.5382 | 3 |
| **Central Obesity** | | | | **Central Obesity** | | | |
| **No** | | Reference | 0 | **No** | | Reference | 0 |
| **Yes** | 1.70 [1.16 – 2.48] | 0.5286 | 2 | **Yes** | 1.70 [1.16 – 2.48] | 0.5296 | 3 |
| | **Max possible points:** | | **18** | | **Max possible points:** | | **23** |
| **DYSGLYCEMIA** | | | | | | | |
| **MODEL 1** | | | | **MODEL 2** | | | |
| **Intercept** | | -1.3268 | | **Intercept** | | -1.3782 | |
| **Age:** | | | | **Age:** | | | |
| **20-29:** | | Reference | 0 | 20-29: | | Reference | 0 |
| **30-39:** | 1.71 [1.19 – 2.46] | 0.5377 | 3 | 30-39: | 1.72 [1.19 – 2.47] | 0.5405 | 5 |
| **40-49:** | 2.41 [1.67 – 3.48] | 0.8805 | 5 | 40-49: | 2.36 [1.64 – 3.40] | 0.8583 | 9 |
| **50-59:** | 4.06 [2.74 – 6.01] | 1.4 | 8 | 50-59: | 4.00 [2.70 – 5.93] | 1.3864 | 14 |
| **60-69:** | 3.40 [2.24 – 5.18] | 1.2247 | 7->8 | 60-69: | 3.21 [2.11 – 4.89] | 1.1667 | 12->14 |
| **70+: *** | 2.82 [1.74 – 4.55] | 1.0351 | 6->8 | 70+: * | 2.61 [1.62 – 4.23] | 0.961 | 10->14 |
| **Had GDM** | | | | **Had GDM** | | | |
| **No** | | Reference | 0 | **No** | | Reference | 0 |
| **Yes** | 2.08 [1.22 – 3.54] | 0.7304 | 4 | **Yes** | 1.95 [1.12 – 3.39] | 0.6691 | 7 |
| **Has/Had HTN** | | | | **Has/Had HTN** | | | |
| **No** | | Reference | 0 | **No** | | Reference | 0 |
| **Yes** | 1.41 [1.10 – 1.80] | 0.3423 | 2 | **Yes** | 1.46 [1.14 – 1.86] | 0.3758 | 4 |
| **BMI** | | | | **Central Obesity** | | | |
| **Normal** | | Reference | 0 | **No** | | Reference | 0 |
| **Overweight** | 1.17 [0.87 – 1.57] | 0.1548 | 1 | **Yes** | 1.54 [1.21 – 1.97] | 0.4317 | 4 |
| **Obese** | 1.70 [1.27 – 2.27] | 0.5279 | 3 | **Gender** | | | |
| | | | | **Male** | | Reference | 0 |
| | | | | **Female** | 1.10 [0.87 – 1.40] | 0.0985 | 1 |
| | **Max possible points:** | | **17** | | **Max possible points:** | | **30** |

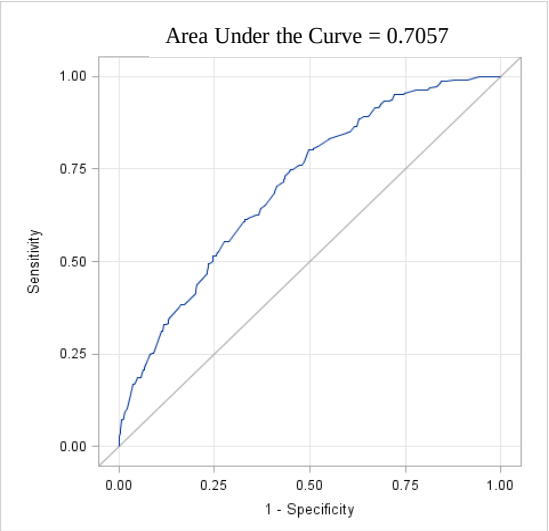
β-coef: β coefficient; Fam Hx DM: Family history of diabetes in parents and siblings; Central Obesity: Waist circumference for women ≥80 cm, men ≥ 94cm (Alberti et al., 2007); BMI: Body Mass Index (underweight or normal [<25.0 kg/m$^2$], overweight [25.0-29.9 kg/m$^2$], and obese [≥30.0 kg/m$^2$] (Alberti et al., 2007)); HTN: Hypertension; GDM: Gestational Diabetes; Smoking: current, former, or never for cigarettes, cigar, pipe, shisha, or guza

**FIGURE 1: RECEIVER-OPERATING CHARACTERISTIC (ROC) CURVES FOR TYPE 2 DIABETES MELLITUS (T2DM) AND DYSGLYCEMIA FINAL MODELS FOR NON-PREGNANT SAUDI ADULTS AGED ≥ 20 YEARS IN 2009 (N=1435)**

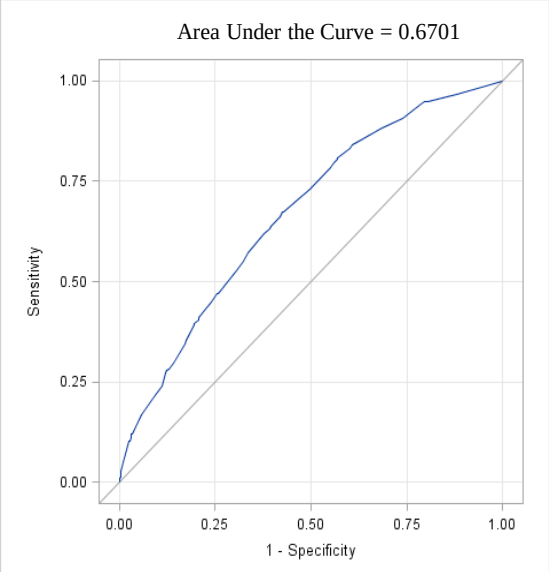
T2DM Model 1:
Age, Sex, Fam Hx DM, GDM, Central Obesity, Smoking



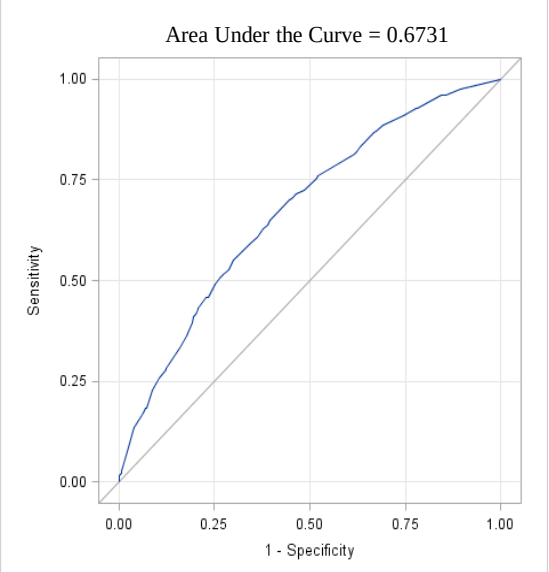

T2DM Model 2:
Age, HTN, GDM, Fam Hx DM, Smoking, Central Obesity




Dysglycemia Model 1:
Age, GDM, HTN, BMI




Dysglycemia Model 2:
Age, GDM, HTN, Sex, Central Obesity




**Legend**
No predictive value (Area Under the Curve = 0.5)
Actual

**Age: Age in 10 year increments (20-29, 30-39, 40-49, 50-59, 60-69, 70+)**
**Fam Hx DM: Family history of diabetes in parents and siblings**
**Central Obesity: Waist circumference for women ≥80 cm, men ≥ 94cm (Alberti et al., 2007)**
**BMI: Body Mass Index (underweight or normal [<25.0 kg/m$^2$], overweight [25.0-29.9 kg/m$^2$], and obese [≥30.0 kg/m$^2$] (Alberti et al.,2007))**
**HTN: Has/Had Hypertension**
**GDM: Had Gestational Diabetes**
**Smoking: Current, former, or never for cigarettes, cigar, pipe, shisha, or guza**

**TABLE 4: PERFORMANCE INDICATORS FOR TYPE 2 DIABETES MELLITUS AND DYSGLYCEMIA RISK SCORES FOR SAUDI NON-PREGNANT ADULTS ≥ 20 YEARS OLD (2009)**

| | Analysis (n=1435) | | | | | Validation (n=50) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Model AUC [95% CI] | HL* | Cut-Off | Sensitivity [95% CI] | Specificity [95% CI] | Model AUC [95% CI] | HL* | Cut-Off | Sensitivity [95% CI] | Specificity [95% CI] |
| **Diabetes** | | | | | | | | | | |
| **Model 1** | 0.7067 [0.6716 – 0.7418] | 0.5580 | >8 | 73.0% [66.5-78.6%] | 56.7% [53.7-59.4%] | 0.6667 [0.5004-0.8329] | 0.0564 | >9 | 88.9% [50.7-99.4%] | 68.3% [51.8-81.4%] |
| **Model 2** | 0.7057 [0.6706 – 0.7407] | 0.7004 | >11 | 67.1% [60.5–73.2%] | 59.1% [56.3–61.9%] | 0.6883 [0.5260-0.8507] | 0.3796 | >11 | 88.9% [50.7–99.4%] | 58.5% [42.2–73.3%] |
| **Dysglycemia** | | | | | | | | | | |
| **Model 1** | 0.6701 [0.6425 - 0.6977] | 0.8131 | >6 | 68.6% [65.9-72.0%] | 56.5% [52.9-60.1%] | 0.7304 [0.5845-0.8763] | 0.0185 | >3 | 84.0% [63.1-94.8%] | 60.0% [38.9-78.2%] |
| **Model 2** | 0.6731 [0.6455 – 0.7006] | 0.5744 | >13 | 64.2% [60.4–67.8%] | 58.9% [55.3-62.4%] | 0.7448 [0.6022-0.8874] | 0.2558 | >10 | 76.0% [54.5-89.8%] | 60.0% [38.9-78.2%] |

***HL:** Hosmer-Lemeshow Test

**Diabetes Model 1:** Age in 10 year increments (20-29, 30-39, 40-49, 50-59, 60-69, 70+), sex, family history of diabetes in parents and siblings (Fam HX DM), had gestational diabetes (GDM), central obesity (waist circumference for women ≥80 cm, men ≥ 94cm (Alberti et al.,2007)), and smoking (current, former, or never for cigarettes, cigar, pipe, shisha, or guza)

**Diabetes Model 2:** Age, GDM, Fam HX DM, central obesity, smoking, and has/had hypertension (HTN)

**Dysglycemia Model 1**: Age, GDM, HTN, and body mass index (underweight or normal [<25.0 kg/m$^2$], overweight [25.0-29.9 kg/m$^2$], and obese [≥30.0 kg/m$^2$] (Alberti et al., 2007))

**Dysglycemia Model 2:** Age, GDM, HTN, sex, central obesity

# CHAPTER 4: CONCLUSION AND RECOMMENDATIONS

Saudi Arabia is a nation that is undergoing rapid transformation. Within the last century, the nation has been catapulted into the forefront of global politics and modern day industrialization with the discovery of oil. The petroleum industry is the largest in the region and the change has been accompanied with increased wealth and life expectancy as well as the influx of fast food restaurants and malls (Alsharekh & Springborg, 2008; Zuhur, 2011). As a result of these major demographic and socioeconomic changes in the population, there has been a transition in nutrition (high quantity and poor quality of dietary intake) and lifestyle patterns (low physical activity) which are associated with increases in chronic disease risk factors (Zuhur, 2011).

The prevalence of obesity in Saudi Arabia has increased over the past few decades. National estimates in 1996 found 40.3% of adult males and 45.5% of adult females were obese or overweight (El-Hazmi & Warsy, 1997). Almost a decade later, national estimates from 2005 showed 66.2% of adult males and 71.4% of adult females were obese or overweight (Ministry of Health Kindom of Saudi Arabia & World Health Organization EMRO, 2005). Adoption of unhealthy dietary habits such as low vegetable and fruit intake and increased consumption of fast food and sugary drinks have also been documented (Collison et al., 2010; Washi & Ageib, 2010). Only a quarter of adolescents consume any vegetables and fruits daily while half rarely or never consume them (Washi & Ageib, 2010). An estimated 90% of adolescents consume food away from home and 85% of the time, fast foods such as pizza, hamburgers, and fried chicken are consumed (Washi & Ageib, 2010). As a result, concurrently, there has been an increase in obesity and other chronic diseases such as T2DM (Al-Daghri et al., 2011; Ng, Zaghloul, Ali, Harrison, & Popkin, 2011).

T2DM is associated with increased morbidity and health care costs and is a precursor for other diseases such as kidney and heart disease (Emerging Risk Factors Collaboration et al., 2010; Goldman & Schafer, 2012; Gu, Cowie, & Harris, 1998; Valensi et al., 2005). In order to address the rising incidence and prevalence of T2DM in the population, a wide range of policies and strategies must be used to tackle the growing problem. For example, strategies that aim at prevention such as education on healthy lifestyles and increasing access to healthcare and treatment may have major impacts on the burdens of diabetes in Saudi Arabia. Detection is an important component of any prevention or treatment strategy for conditions that are asymptomatic during the early phase (like diabetes). However, detection through population wide blood glucose testing can be costly. A more cost-efficient approach is to offer glucose testing to those with a higher likelihood of having the disease, and therefore increasing the yield among those tested. A risk score can help identify those that should be offered glucose testing. Our risk scores facilitate the screening process to identify those who currently have undiagnosed diabetes or dysglycemia. Once identified, the goal is to quickly have them become normaglycemic and to prevent further progression of the disease.

Risk scores are just one tool that is available to address the growing burden of diabetes in the population. However for them to be effective, they need to be used in conjunction with other strategies and have proper resources. Resources such as equipment to measure waist circumference and blood pressure, a laboratory for diagnostic testing, and adequate staff to obtain measurements are needed to implement the risk score. In addition, training for both physicians and other care providers is needed to ensure proper utilization of the risk score as well as to implement interventions to prevent the progression and onset of diabetes. A cross-sectional study in 2010 found moderate gaps in knowledge, attitudes, and practices among primary care

physicians regarding T2DM. The study estimated that 28.3% of the physicians surveyed did not know the diagnostic criteria for T2DM and 86.8% did not consider Diabetes Self-Management Education (DSME) to be an important part of care (Khan et al., 2011). DSME is a collaborative approach to educate and empower patients to manage their diabetes (American Diabetes Association, 2013; Haas et al., 2012). DSME is an example of how patient education is a crucial component of management for any disease.

The last study performed on the knowledge, attitudes, and practices of those with diabetes in Saudi Arabia was in 1992 and showed low levels of knowledge, attitude, and compliance (Binhemd, 1992). Hence, a greater emphasis on patient education in both the clinical and community setting is needed. Further qualitative research assessing providers and community members on their knowledge, attitude, and practices regarding T2DM needs to be performed to further illuminate the current gaps in patient care. Other interventions need to address physical activity and dietary habits and the greater socio-contextual environmental factors that affect these lifestyle choices such as the lack of access to gyms and Saudi Arabia's extremely hot weather. Research can help identify innovative ways to facilitate these lifestyle changes in the context of Saudi Arabia. In addition, strategies are needed to ensure linkage of care from screening to diagnostic testing, to health education, and to treatment by health care providers and adequate follow up. It is only with this sort of multi-pronged attack that involves the government, public, community, and health care providers that we can stem the growing tide of T2DM and its morbidity.

*References*

Al-Daghri, N. M., Al-Attas, O. S., Alokail, M. S., Alkharfy, K. M., Yousef, M., Sabico, S. L., & Chrousos, G. P. (2011). Diabetes mellitus type 2 and other chronic non-communicable diseases in the central region, Saudi Arabia (Riyadh cohort 2): a decade of an epidemic. *BMC Med, 9*, 76. doi: 10.1186/1741-7015-9-76

Alsharekh, Alanoud, & Springborg, Robert. (2008). *Popular Culture and Political Identity in the Arab Gulf States*. Lebanon: London Middle East Institute at SOAS.

American Diabetes Association. (2013). Standards of medical care in diabetes--2013. *Diabetes Care, 36 Suppl 1*, S11-66. doi: 10.2337/dc13-S011

Binhemd, T. A. (1992). Diabetes mellitus: Knowledge, attitude, practice and their relation to diabetes control in female diabetics. *Ann Saudi Med, 12*(3), 247-251.

Collison, K. S., Zaidi, M. Z., Subhani, S. N., Al-Rubeaan, K., Shoukri, M., & Al-Mohanna, F. A. (2010). Sugar-sweetened carbonated beverage consumption correlates with BMI, waist circumference, and poor dietary choices in school children. *BMC Public Health, 10*, 234. doi: 10.1186/1471-2458-10-234

El-Hazmi, M. A., & Warsy, A. S. (1997). Prevalence of obesity in the Saudi population. *Ann Saudi Med, 17*(3), 302-306.

Emerging Risk Factors Collaboration, Sarwar, N., Gao, P., Seshasai, S. R., Gobin, R., Kaptoge, S., . . . Danesh, J. (2010). Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies. *Lancet, 375*(9733), 2215-2222. doi: 10.1016/S0140-6736(10)60484-9

Goldman, Lee, & Schafer, Andrew. (2012). *Goldman's Cecil Medicine* (24th ed.). United States of Ameria: Elsevier.

Gu, K., Cowie, C. C., & Harris, M. I. (1998). Mortality in adults with and without diabetes in a national cohort of the U.S. population, 1971-1993. *Diabetes Care, 21*(7), 1138-1145.

Haas, L., Maryniuk, M., Beck, J., Cox, C. E., Duker, P., Edwards, L., . . . Youssef, G. (2012). National standards for diabetes self-management education and support. *Diabetes Educ, 38*(5), 619-629. doi: 10.1177/0145721712455997

Khan, A. R., Al Abdul Lateef, Z. N., Khamseen, M. B., Al Aithan, M. A., Khan, S. A., & Al Ibrahim, I. (2011). Knowledge, attitude and practice of ministry of health primary health care physicians in the management of type 2 diabetes mellitus: a cross-sectional study in the Al Hasa District of Saudi Arabia, 2010. *Niger J Clin Pract, 14*(1), 52-59. doi: 10.4103/1119-3077.79241

Ministry of Health Kindom of Saudi Arabia, & World Health Organization EMRO. (2005). WHO STEPwise Approach to NCD Surveillance Country-Specific Standard Report: Saudi Arabia.

Ng, S. W., Zaghloul, S., Ali, H. I., Harrison, G., & Popkin, B. M. (2011). The prevalence and trends of overweight, obesity and nutrition-related non-communicable diseases in the Arabian Gulf States. *Obes Rev, 12*(1), 1-13. doi: 10.1111/j.1467-789X.2010.00750.x

Valensi, P., Schwarz, E. H., Hall, M., Felton, A. M., Maldonato, A., & Mathieu, C. (2005). Pre-diabetes essential action: a European perspective. *Diabetes Metab, 31*(6), 606-620.

Washi, S. A., & Ageib, M. B. (2010). Poor diet quality and food habits are related to impaired nutritional status in 13- to 18-year-old adolescents in Jeddah. *Nutr Res, 30*(8), 527-534. doi: 10.1016/j.nutres.2010.07.002

Zuhur, Sherifa. (2011). *Saudi Arabia*. USA: ABC-CLIO, LLC.