Glycemic Control and Accompanying Risk Factors: 4-Year Primary Care Study

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Abstract

Objective: This study is to assess the glycemic control and the other risk factors like LDL, blood pressure readings and body mass index for type 2 diabetes mellitus (T2DM) in 8 primary care centers over 4 years of time.

Methods: An observational, retrospective cohort, multicenter study which was conducted in 8 National Guard primary health care centers. Four of the centers were located in Riyadh; while the others are from different regions in Saudi Arabia. A stratified random sampling method was used according to number of diabetic patients at each center.

The main study outcomes were to measure the mean HbA1c, LDL levels, blood pressure and BMI readings and the percentage of diabetic patients who reached the ADA goal of HbA1c, LDL, and blood pressure and how it changed during 4 years of time. Also the percentage of adults with diabetes who have HbA1c<0.07 and the changes of controlled patients within the study period.

Results: Total number of type-2 diabetic patients of this study was 778, with mean age of 55.03 ± 11.4, 62.7% of them were females. The mean of the HbA1c was 8.7 on 2006 and reduced to 8.6 within four years, 16.6% of diabetic patients had their last HbA1c reading reached the HbA1c goal (≤7%). The LDL and diastolic blood pressure decreased also within the follow up years insignificantly (-0.299 and -1.37). While the systolic blood pressure and BMI increased over 4 years of time (+0.58 and +0.27). HbA1c level shows a significant relation with the education levels in 2007 and 2008. HbA1c also prove a significant relation with LDL for three years in sequence. Age and BMI had a significant relation with the systolic blood pressure.

Conclusion: Poor glycemic control has serious impact not only on patients but on the society. The primary health care setting and structure were not well-prepared to properly manage diabetes and its related comorbidities.

Keywords: Diabetes mellitus; HbA1c; Glycemic control; Quality of care; Risk factors; Hypertension; Obesity; Dyslipidemia; High lipid

Introduction

Diabetes is a chronic disease with complex causes, manifestations, complication, and management. It is a chronic disease which is considered a major cause of death, illness and reduce quality of life [1]. Diabetes is gradually becoming a global health issue. The disease imposes huge public health and economic burdens that affect the society before the individuals. As estimated by International Diabetes Federation, there were 366 million people suffering from diabetes worldwide in 2011, and most probably by 2030 this figure will rise to 552 million. Diabetes also caused 4.6 million deaths and at least 465 billion US dollars in healthcare expenditures [2]. Moreover, the prevalence of type 2 diabetes is also increasing dramatically in the Middle East and North Africa region [3].

Type 2 diabetes is known to be a disease of disordered lipid metabolism as well as a disease of abnormal glucose metabolism [4]. Hemoglobin A1c (HbA1c) is a standard measure of glycaemia over 2–3 months [5]. Nowadays, there is a contemporary tendency to focus on HaemoglobinA1c (HbA1c) rather than Fasting Plasma Glucose (FPG) or oral glucose tolerance test (OGTT) in the diagnosis of diabetes [6].

It was proved that patients with HbA1c ≥ 6.5% have more critical cardiovascular and metabolic risks than those with HbA1c<6.5%, especially in OGTT-negative population. This is clinically important because it indicates that patients with HbA1c ≥ 6.5% and normal OGTT may not be at low hazard as previously thought, and more intensive management should be preceded. Also an increase of 1% in HbA1c is associated with an approximately 40% increased risk of coronary heart disease and 30% increased risk of all-cause mortality after adjusting for
other risk factors [7]. There are many factors causing the poor control of diabetes related to patients, healthcare professionals and health care system [8].

HbA1c testing should be performed routinely in all patients with diabetes; first, to document the degree of glycemic control at initial assessment, and second, as part of continuing care. The HbA1c level for patients to maintain in general is to be of <7%. Lowering HbA1c has been associated with a reduction of many microvascular and neuropathic complications of diabetes [9-12]. But there is a deficiency treating the diabetic patients especially in the developing countries.

This study aimed to assess glycemic control and changes in glycemic control and other risk factors over 4 years in patients with type 2 diabetes mellitus (T2DM) treated at primary health setting.

**Literature Review**

Type-2 Diabetes mellitus presents an epidemic proportions in Saudi Arabia, throughout the country with exceedingly high rates concentrated in urban areas [13]. A national survey indicates that the overall prevalence of DM is 23.7%. [14,15] and despite the readily available access to healthcare facilities, a large number of diabetics, 27.9%, were unaware of having DM [16]. A recent national study found that diabetes mellitus affects 1,745,532 persons with prevalence of 13.45%, 16.6% of them were adequately controlled (HbA1c of ≤ 7%) [17].

The majority of diabetic patients are not receiving recommended levels of healthcare [18-20] and there is large variation in how often people with diabetes receive these recommendations. There are 20-90% of diabetics who receive an HbA1c test annually, those who have HbA1c levels <7% are 12-40% [21-23], nearly one-third do not have a retinal examination; foot examinations were not documented for 33-94% of patients. Additionally, many patients had elevated and untreated hypertension and lipid abnormalities [24].

There is accumulated evidence from well conducted studies confirming the relationship between proper glycemic control and reduction or prevention of diabetic complications. UKPDS showed that patients receiving intensive treatment over 10 years had 11% decrease HbA1c and 10% reduction in any diabetes-related complication [9,11,25-27].

However, the percentage of patients who reached the glycemic goal vary between studies, but generally it is unexpectedly low. It ranges between 15-50% [17].

**Materials and Methods**

**Study design**

An observational, retrospective cohort study conducted between 1st January 2006 and 31st December 2009.

**Study setting**

The study was conducted on medical records collected from 8 primary health care centers belonging to National Guard Health Affairs-Saudi Arabia. Four of the targeted centers were located in the capital of Riyadh and the other 4 are in Qassim, Arar, Rafha, and Najran.

**Study subjects**

The study included only charts of patients who were 18 years old or older and are known to have type II diabetes mellitus, who received any type of anti-diabetic treatment. Records lacking follow up notes of 12 months or more between 2006 and 2009 were excluded from the study. Also, records that indicate patient refusal to accept treatment or discontinuation of management against medical advice during this period were excluded from the study.

**Sampling method and sample size calculation**

Records of diabetic subjects in the primary care centers represented the sampling frame. Stratified sampling method was used. Each of the 8 targeted primary care centers was considered a stratum and sampled using simple random sampling method. After calculating the total sample size required, the number of records obtained from each center was calculated in proportion to the total number of diabetics served by that center.

The total number of diabetics in all the clinics was estimated to be 200,000 based on 20.22% prevalence of adult diabetes mellitus in Saudi Arabia (IDF country records). The sample size was calculated based on the percent of diabetic patients with optimum Hba1c of 7.0 or less. We assumed that 50% of diabetics in our clinics have well controlled diabetes. Using a 95% confidence interval, margin of error of 4% and 1.5 design effect (this will increase the sample size by 50% to account for imperfections in the sampling method) the sample size was calculated using open-Epi online epidemiologic calculator. The calculator used can be accessed online at: http://www.openepi.com/SampleSize/SSPropor.html

The total number of records required for the study was 898 of which 120 were excluded due to incomplete data. The total number of records included in the analysis was 778.

**HbA1c, LDL, HDL determination**

Measurement of HbA1c is key in monitoring and long-term management of patients with diabetes, thus its measurement should be optimally accurate and precise. Recent developments in medical technology allow clinicians to determine HbA1c test results during a patient’s office visit. Several manufacturers offer an assay that can be done by trained medical staff and yield HbA1C results in minutes. The National Glycohemoglobin Standardization Program (NGSP) certifies methods annually at the manufacturer level. Every laboratories should use only HbA1C assay methods that are certified by the (NGSP).

The guideline shows that, the desirable specifications for Hb A1C measurement are an intralaboratory coefficient of variation (CV) should be less than 2% and an interlaboratory (CV) should be less than 3.5%.

**LDL:** Our laboratory is using the MULTIGENT Direct LDL assay; it is a homogeneous method for directly measuring LDL levels in serum or plasma, without the need for off-line pretreatment or centrifugation steps. This detergent solubilizes only the non-LDL particles. The cholesterol released is consumed by cholesterol esterase and cholesterol oxidase in a non-color-forming reaction. A second detergent solubilizes the remaining LDL particles and a chromogenic coupler allows for color formation. The enzyme reaction with LDL in the presence of the coupler produces color that is proportional to the amount of LDL cholesterol present in the sample.

**HDL:** Our laboratory is using the Ultra HDL assay; it is a homogeneous method for directly measuring HDL cholesterol concentrations in serum or plasma without the need for off-line
pretreatment or centrifugation steps. The method uses a two-reagent format and depends on the properties of a unique detergent.

**Data collection**

Data were collected using data collection form created by the authors of the study. The form included non-identifying patient demographics, patient lab records (biomarkers) and associated comorbidities. Data collection staff received special training to be able to use the form and record the data in a standardized manner. Data collection was conducted between March 2010 and May 2011.

**Data management**

IBM Statistical Package for Social Science (SPSS) version 20 was used for data entry and analysis. Data were entered into a unified SPSS database by trained data entry clerks.

**Data analysis**

Categorical variables were summarized using simple frequency and percentage. Continuous variables summarized using arithmetic mean and standard deviation.

Comparing proportions was performed principally using Chi square test. Fisher exact test was used when the assumptions for Chi square were violated.

Comparing two means was carried out using independent group student t-test. ANOVA was used to compare more than two means when needed. When significant differences detected by ANOVA, Post Hoc analysis was carried out using Bonferroni test.

All statistical tests were bidirectional. Statistical significance was set to 0.05 or less for all statistical tests.

**Results**

**Socio-demographic characteristics**

The study included 778 patients from 8 primary care centers inside Saudi Arabia. The mean age of patients was 55.03 ± 11.4; the highest percentage of age group is 51-64 (41.51%), then 31-50 (36.81%). Elderly people >65 years old is 20.7%, and female patient is predominant 62.7%. Most study subjects were married 89.4%, illiterate 55.6%, and housewives 39.2%.

**HbA1c**

The mean HbA1c reduced from 8.75 (2006) to 8.63 (2009) with no significant difference (P value of T-test = 0.147).

Diabetic patients who reached the HbA1c goal increased from 12.6% in 2006 to 16.6% in 2009 with P value<0.00, while the poorly controlled (HbA1c>0.09) reduced from 63.8% in 2006 to 46.9% in 2009 with P value<0.001 (chi square test), reduction is consistent through the 4 years follow-up (Figure 1).

Graphs showing the trend of HA1c, LDL, HDL levels trend through years.

Graphs showing the trend of SBP, DBP, BMI levels trend through years.

**Figure 1**: Four Year’s Trend for 6 important variables.
LDL

The mean LDL was 3.08 (2006) reduced to 2.8 (2009). Those who reached the LDL goal (LDL ≤ 2.6) was around 53% over the 4 years with a significant difference between groups in the beginning to the end of the study with P value of chi-square <0.00.

SBP and DBP

The mean SBP was 129.8 ± 19.2 (2006) increased to 130.4 ± 17.50 (2009).

Diabetic patients who were uncontrolled (SBP ≥ 130) were increased over the 4 years of follow-up, from 28.9% (2006) to 39.6 (2009). Uncontrolled Systolic Blood Pressure increased too from 17.4 of the sample in (2006) to 19.9 (2009). While the mean DBP in general was 77.29 (2006) reduced to 76.42 (2009), both variables differences between 2006 and 2009 are significantly different with P value of <0.00.

BMI

The mean BMI was 32.16 ± 5.9 (2006) which increased to 32.43 ± 5.7 (2009). The percentage of obesity increased during the years of follow-up from 40.2% (2006) to 48.4% (2009). The difference gave a significant difference P value of chi-square <0.00.

HbA1c relationships

HbA1c 2006 and 2009 had no significant relationships with sex, age, education or BMI levels. While in 2007 and 2008, it is showing a significant relationship with education level with P value of Chi-square test <0.01. HbA1c had significant relationship with LDL in 2006, 2007 and 2008 excluding 2009 with P value of Chi-square test <0.001.

SBP has significant relationship with age groups in 2006 to 2009 with a P value of One way Anova <0.001, also with BMI in 2006 and 2007 P value Chi-square test (<0.005 - 0.020) and HbA1c in 2008 P value (0.032). These results were also presented in linear graph (Figure 1). Number of diabetic patient who had annual eye and foot examination increased from 30% (2006) to almost 50% (2009) presented in Figure 2.

Figure 3 shows that the oral hypoglycemic drugs were highly used
Discussion

Our study showed that 16.6% of diabetic patients were adequately controlled (last HbA1c reading at 2009 of ≤ 7.0%), while the mean in the 4 years follow-up is 13.55%. This is similar to the results of a recent national study in Saudi Arabia which showed that 16.6% were adequately controlled (HbA1c of ≤ 7%) [17]. These findings were far less than RECAP-DM study findings were 27% of diabetic patients in 7 European countries have HbA1c of <6.5%, (RECAP study) and 31% in CODE study and 33.5% in US study [28,29]. Other study showed even better HbA1c readings which reached up to 47% [30,31].

Although the overall percentage of adequately controlled patients was low (16.6% last reading at 2009) compared to other studies, the percentage of poorly controlled diabetic patients (HbA1c>9.0%) was reduced over the follow up period of the study from 63.8% (2006) to 46.9% (2009), a reduction of ~16.7% in 4 years duration. However, the mean HbA1c was almost similar during the study period (8.75 at 2006 to 8.63 at 2009), [32] found that the mean HbA1c of 7.6 ± 1.6. This was lower than our study’s findings.

The barriers behind the poor control of diabetes in our setting were many, but they can be grouped into health professional factors, patient’s factors, health system factors and disease factors.

Diabetes is a progressive disease due to gradual decline in mass and function of B-cells in the pancreas, which requires PHC physicians to intensify the medication prescribed to their patients from OHD to insulin therapy.

Primary care physicians are at the frontline in providing the best care to diabetic patients because they encounter and manage more diabetic patients than the diabetologists. However, there are many factors affecting this role [33,34], early insulin initiation in the course of diabetic management of poorly controlled cases has been proven to reduce and prevent the long-term diabetes complications [35-37]. However, there was delay and underuse in insulin therapy, as 83% of study participants were uncontrolled, however 10% only were on insulin therapy (Tables 1-3). Studies showed that insulin initiation was delayed for two to five years after trials and failures of oral hypoglycemic medications [26,38]. One substantial factor is the Psychological Insulin Resistance (PIR), defined as psychological resistance towards insulin therapy, among patients and health care providers [8,39].

Diabetes is a silent disease, patients need to be monitored and reinforced on a regular basis and enrolled in a structured diabetic care program at PHC settings. The program includes periodic assessment and a regular complication screening by a diabetes team and enforcing diabetic self-care program. Such programs reduced HbA1c from 8.4 to 6.9 and increased the adequately controlled HbA1c from 30% to 63% in one year duration [27,40,41].

The mean LDL was reduced from 3.1 mmol/dl (2006) to 2.8 mmol/dl (2009), a change of only -0.3 mmol/dl and almost half (52.5%) of diabetic patients had their LDL reached the goal (LDL<2.6 mmol/dl) in 2006. This percentage was almost maintained during the follow-up period. Studies showed wide variation of the percentage of those who reached the LDL goal (15% to 87%) [30,31]. The problem in our study in addition to the modest control of LDL was that our PHC providers failed to make significant change in the number of controlled patients, dislike the findings of Ackermann study who reported the positive change of 20.5% [42].

### Table 1: Patient's socio-demographic characteristics.

| Variable        | No  | %   |
|-----------------|-----|-----|
| Age             |     |     |
| 30 and less     | 8   | 1   |
| 31-50           | 286 | 36.8|
| 51-64           | 323 | 41.5|
| 65 and more     | 161 | 20.7|
| Sex             |     |     |
| Male            | 293 | 37.3|
| Female          | 493 | 62.7|
| Marital Status  |     |     |
| Single          | 15  | 1.9 |
| Married         | 707 | 89.4|
| Divorced        | 8   | 1   |
| Widow           | 61  | 7.7 |
| Education Level |     |     |
| Illiterate      | 429 | 55.6|
| Primary         | 223 | 28.9|
| Intermediate    | 45  | 5.8 |
| Secondary       | 47  | 6.1 |
| University graduate | 27 | 3.5 |
| Occupation      |     |     |
| Teacher         | 10  | 1.3 |
| Military        | 141 | 17.8|
| Unemployed      | 311 | 39.2|
| Retired         | 114 | 14.4|
| Others          | 217 | 27.4|

Unfortunately, there was deterioration of the percentage of diabetic patients who had their systolic BP controlled (from 71.1% in 2006 to 66.4% in 2009), this was in contrast to the findings of one study which reported that 6.4% had positive change [42]. Diabetics who had ideal systolic BP varies between 29% to 73% [30,31,43].

Obesity is progressively worsened among diabetic patients which may be due to insulin therapy and other medication, poor glycemic control and diabetic complications [44,45].

When associated with diabetes, obesity may cause insulin resistance, hypertension, increased risk of cardiovascular diseases and other complications of obesity [46].

On the other hand, weight reduction improves diabetes and the need for anti-diabetic medication [47]. Obesity and overweight were progressively increased among our patients in the expense of normal weight patients. Obesity increased from 40.5% (2006) to 48.4% (2009), this finding was much higher than other studies [47,48].

**Conclusion**

Diabetes affects the community in two ways. First, its prevalence increases, and second, its severity increases and become more aggressive during the course of the disease. It is evident that proper controlling of diabetes, obesity, LDL and hypertension reduce diabetic complications. The current primary health care centers’ structure to properly manage diabetes and the other related risk factors is suboptimal.

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Table 2: Percentage per year of important variables’ categories for 4 years.

| Variable       | 2006       | 2007       | 2008       | 2009       | *P value |
|----------------|------------|------------|------------|------------|----------|
|                | No. %      | No. %      | No. %      | No. %      |          |
| HA1c           |            |            |            |            |          |
| Target <= 0.07 | 100 12.6   | 91 11.5    | 107 13.5   | 132 16.6   | 0.000    |
| Optimal (controlled) <= 0.08 | 98 12.4 | 124 15.6 | 138 17.4 | 164 20.7 |          |
| Uncontrolled >0.08 - < 0.09 | 89 11.2 | 101 12.7 | 120 15.1 | 125 15.8 |          |
| Poorly controlled > 0.09 | 505 63.8 | 477 60.2 | 428 54.0 | 372 46.9 |          |
| LDL            |            |            |            |            |          |
| Controlled <= 2.6 | 416 52.5 | 433 54.6 | 434 54.7 | 420 53.0 | 0.000    |
| Uncontrolled > 2.6 | 377 47.5 | 460 45.4 | 359 45.3 | 373 47.0 |          |
| SBP            |            |            |            |            |          |
| Controlled <= 130 | 564 71.1 | 565 71.2 | 500 63.1 | 479 60.4 | 0.000    |
| Uncontrolled > 130 | 229 28.9 | 228 28.8 | 293 36.9 | 314 39.6 |          |
| DBP            |            |            |            |            |          |
| Controlled <= 85 | 655 82.6 | 656 82.7 | 644 81.2 | 635 80.1 | 0.000    |
| Uncontrolled > 85 | 138 17.4 | 137 17.3 | 149 18.8 | 158 19.9 |          |
| BMI            |            |            |            |            |          |
| Normal         | 260 36.6   | 223 32     | 199 29.3   | 166 24.7   | 0.000    |
| Overweight     | 163 22.9   | 163 23.4   | 171 25.1   | 180 26.8   |          |
| Obese1         | 164 23.1   | 177 25.4   | 175 25.7   | 180 26.8   |          |
| Obese2         | 75 10.5    | 79 11.3    | 79 11.6    | 89 13.3    |          |
| Morbid Obesity | 49 6.9     | 55 7.9     | 56 8.2     | 56 8.3     |          |
| Creatinin      | 83.5316 51.79371 | 80.7730 19.12130 | 79.6151 49.83476 | 76.0155 45.65241 | 0.034 |

Table 3: Mean and standard deviation per year of important variables’ categories for 4 years.

| Variable       | 2006       | 2007       | 2008       | 2009       | *P value |
|----------------|------------|------------|------------|------------|----------|
|                | Mean  SD   | Mean  SD   | Mean  SD   | Mean  SD   |          |
| HA1c           |            |            |            |            |          |
| .08750 .019081 | .08799 .018759 | .08710 .018627 | .08682 .019376 | .0147 |
| LDL            | 3.07523 .949100 | 2.90858 .922470 | 2.79688 .827124 | 2.77625 .888498 | 0.000 |
| SBP (last reading) | 129.78 19.175 | 128.66 18.876 | 130.79 18.030 | 130.36 17.502 | 0.867 |
| DBP (last reading) | 77.79 8.899 | 76.67 9.052 | 76.73 9.371 | 76.42 9.241 | 0.000 |
| BMI            | 32.16 5.907 | 32.22 5.894 | 32.36 5.856 | 32.43 5.793 | 0.002 |
| BUN            | 5.080 1.4800 | 5.115 2.2203 | 4.962 1.7366 | 5.158 2.3898 | 0.118 |
| Creatinin      | 83.5316 51.79371 | 80.7730 19.12130 | 79.6151 49.83476 | 76.0155 45.65241 | 0.034 |

financially gain or lose from publishing this study. Moreover, there are no patents relating to the content of the manuscript.

References

1. Narayan KM, Benjamin E, Gregg EW, Norris SL, Engelgau MM (2004) Diabetes translation research: where are we and where do we want to be? Ann Intern Med 140: 958-963.
2. Peng G, Lin M, Zhang K, Chen J, Wang Y, et al. (2013) Hemoglobin A1c can identify more cardiovascular and metabolic risk profile in OGTT-negative Chinese population. Int J Med Sci 10: 1028-1034.
3. Shihabi AR, Moussa EM, Sobierajska H, Schmidt B (2013) An observational study of acarbose treatment in patients with type 2 diabetes from the Middle East and Morocco. Diabetes Metab Syndr Obes 6: 141-150.
4. Johannsen NM, Sparks LM, Zhang Z, Earnest CP, Smith SR, et al. (2013) Determinants of the Changes in Glycemic Control with Exercise Training in Type 2 Diabetes: A Randomized Trial. PLoS One 8: e62973.
5. Christman AL, Selvin E, Margolis DJ, Lazarus GS, Garza LA (2011) Hemoglobin A1c predicts healing rate in diabetic wounds. J Invest Dermatol 131: 2121-2127.
6. Steele AM, Wensley KJ, Ellard S, Murphy R, Shepherd M, et al. (2013) Use of HbA1c in the identification of patients with hyperglycemia caused by a glucokinase mutation: observational case control studies. PLoS One 8: e65326.
7. Guisasola FA, Mavros P, Nocega A, Alemao E, Alexander C, et al. (2008) Glycaemic control among patients with type 2 diabetes mellitus in seven European countries: findings from the Real-Life Effectiveness and Care Patterns of Diabetes Management (RECAP-DM) study. Diabetes Obes Metab 10: 8-15.
8. Lee YK, Lee PY, Ng CJ (2012) A qualitative study on healthcare professionals’ perceived barriers to insulin initiation in a multi-ethnic population. BMC Fam Pract 13: 28.
9. Nicolerat JA (2000) Implications of the United Kingdom Prospective Diabetes Study (UKPDS) results on patient management. Diabetes Educ 26 Suppl: 8-10.
10. Orozco Beltran D, de la Sen Fernandez C, Guillem VG, Munuera CC, Perez JN (2010) [Diabetes mellitus and cardiovascular risk. Is integrated therapy of type 2 diabetes and cardiovascular risk factors necessary?]. Aten Primaria 42: 16-23.
11. Tanaka S, Iimuro S, Yamashita H, Katayama S, Akanuma Y, et al. (2013) Predicting macro- and microvascular complications in type 2 diabetes: the Japan Diabetes Complications Study/the Japanese Elderly Diabetes Intervention Trial risk engine. Diabetes care 36: 1193-1199.
12. Gennuth S (2008) The UKPDS and its global impact. Diabet Med 25 Suppl 2: 57-62.
13. LaKind JS, Naiman DQ (2010) Daily intake of bisphenol A and potential sources of exposure: 2005–2006 National Health and Nutrition Examination Survey. J Expo Sci Environ Epidemiol 21: 272-279.
14. Ali-Nozha MM, Al-Maatouq MA, Al-Mazrou YY, Al-Harthi SS, Arafah MR, et al. (2004) Diabetes mellitus in Saudi Arabia. Saudi Med J 25: 1603-1610.
15. Al-Hazmi MA, Warzy AS, Al-Swailm AR, Al-Swailm AM, Sulaimani R, et al. (1996) Diabetes mellitus and impaired glucose tolerance in Saudi Arabia. Ann Saudi Med 16: 381-385.
16. Rothman R, Malone R, Bryant B, Horlen C, DeWalt D, et al. (2004) The Rothman Risk engine. Diabetes care 36: 1193-1199.
17. El Bcheraoui C, Basulaiman M, Tuffaha M, Daoud F, Robinson M, et al. (2014) Determinants of the Changes in Glycemic Control with Exercise Training in Type 2 Diabetes: A Randomized Trial. PLoS One 8: e62973.
Status of the diabetes epidemic in the Kingdom of Saudi Arabia, 2013. Int J Public Health 59: 1011-1021.

18. Kenny SJ, Smith PJ, Goldschmidt MG, Newman JM, Herman WH (1993) Survey of physician practice behaviors related to diabetes mellitus in the US: Physician adherence to consensus recommendations. Diabetes care 16: 1507-1510.

19. Edelman D, Matchar DB, Oddone EZ (1996) Clinical and radiographic findings that lead to intervention in diabetic patients with foot ulcers. A nationwide survey of primary care physicians. Diabetes Care 19: 755-757.

20. American Diabetes Association (2006) Standards of medical care in diabetes--2006. Diabetes Care 29 Suppl 1: S4-42.

21. Department of Health and Human Services, Centers for Disease Control and Prevention (2003) Control CFD, Prevention. National diabetes fact sheet: general information and national estimates on diabetes in the United States, 2005. Atlanta, GA, US.

22. [No authors listed] (2003) Glycohemoglobin analyzers. Health Devices 32: 409-435.

23. Schiel R, Hoffmann A, Müller UA (1989) Quality of care of patients with diabetes mellitus living in a rural area of Germany. Med Klin (Munich) 94: 127-132.

24. Peters AL, Legorreta AP, Ossorio RC, Davidson MB (1996) Quality of outpatient care provided to diabetic patients. A health maintenance organization experience. Diabetes Care 19: 601-606.

25. Holman RR, Paul SK, Bethel MA, Matthews DR, Neil HA (2008) 10-year follow-up of intensive glucose control in type 2 diabetes. N Engl J Med 359: 1577-1589.

26. Nichols GA, Koo YH, Shah SN (2007) Delay of insulin addition to oral combination therapy despite inadequate glyemic control: delay of insulin therapy. J Gen Intern Med 22: 453-458.

27. Health Quality Ontario (2009) Community-based care for the management of type 2 diabetes: an evidence-based analysis. Ont Health Technol Assess Ser 9: 1-40.

28. Koro CE, Bowlin SJ, Bourgeois N, Fedder DO (2004) Glycemic control from 1988 to 2000 among U.S. adults diagnosed with type 2 diabetes: a preliminary report. Diabetes Care 27: 17-20.

29. Saydah SH, Fradkin J, Cowie CC (2004) Poor control of risk factors for vascular disease among adults with previously diagnosed diabetes. JAMA 291: 335-342.

30. Yong TY, Philibert G, Phillips PJ (2007) Management outcomes of patients with type 2 diabetes: targeting the 10-year absolute risk of coronary heart disease. Med J Aust 186: 622-624.

31. Wan Q, Harris MF, Jayasinghe UW, Flack J, Georgiou A, et al. (2006) Quality of diabetes care and coronary heart disease absolute risk in patients with type 2 diabetes mellitus in Australian general practice. Qual Saf Health Care 15: 131-135.

32. Charpentier G, Genes N, Vaur L, Amar J, Clerson P, et al. (2003) Control of diabetes and cardiovascular risk factors in patients with type 2 diabetes: a nationwide French survey. Diabetes Metab 29: 152-158.

33. Kruger DSG (2009) Addressing barriers to timely intensification of diabetes care: the relationship between clinical inertia and patient behaviour. Consultant 49: S20--S25.

34. (2000) Attitudes of Italian physicians towards intensive metabolic control in Type 2 diabetes. The QuEED Study Group-Quality of Care and Outcomes in Type 2 Diabetes. Diabetes Nutr Metab 13: 149-155.

35. Hanefeld M, Bramlage P (2013) Insulin use early in the course of type 2 diabetes mellitus: the ORIGIN trial. Curr Diab Rep 13: 342-349.

36. Westphal SA, Palumbo J (2006) A case for introducing insulin early in the treatment of type 2 diabetes mellitus. Insulin 1: 65-69.

37. Vinik A (2007) Advancing therapy in type 2 diabetes mellitus with early, comprehensive progression from oral agents to insulin therapy. Clinical therapeutics 29: 1236-1253.

38. Rubino A, McQuay LJ, Gough SC, Kvasz M, Tennis P (2007) Delayed initiation of subcutaneous insulin therapy after failure of oral glucose-lowering agents in patients with Type 2 diabetes: a population-based analysis in the UK. Diabetic Med 24: 1412-1418.

39. Hassan HA, Tohid H, Amin RM, Bidin MBL, Muthupalaniappen L, et al. (2013) Factors influencing insulin acceptance among type 2 diabetes mellitus patients in a primary care clinic: a qualitative exploration. BMC Fam Pract 14: 164.

40. Periodic education from dietitians, diabetes nurses and the importance of a regular complication screening every 12 - 16 months.

41. Chevreul K, Brunn M, Cadier B, Nolte E, Durand-Zaleski I (2014) Evaluating structured care for diabetes: can calibration on margins help to avoid overestimation of the benefits? An illustration from French diabetes provider networks using data from the ENTRED Survey. Diabetes care 37: 1892-1899.

42. Ackermann EW, Mitchell GK (2006) An audit of structured diabetes care in a rural general practice. Med J Aust 185: 69-72.

43. Lu SE, Beckles GL, Crosson JC, Bilk D, Karter AJ, et al. (2012) Evaluation of risk equations for prediction of short-term coronary heart disease events in patients with long-standing type 2 diabetes: the Translating Research into Action for Diabetes (TRIAD) study. BMC endocrine disorders 12: 12.

44. Campbell L, Rössner S (2001) Management of obesity in patients with Type 2 diabetes. Diabet Med 18: 345-354.

45. Magnani L (2001) [Obesity and diabetes mellitus]. Minerva Gastroenterol Dietol 47: 223-226.

46. Mannan MA, Rahman MS, Siddiqui NI (2004) Obesity management in patients with type 2 diabetes mellitus. Mymensingh Med J 13: 95-99.

47. Gagliardi L, Wittert G (2007) Management of obesity in patients with type 2 diabetes mellitus. Curr Diabetes Rev 3: 95-101.

48. Gomes MB, Giannella-Neto D, Faria M, Tambascia M, Fonseca RM, et al. (2009) Estimating cardiovascular risk in patients with type 2 diabetes: a national multicenter study in Brazil. Diabetol Metab Syndr 1: 22.