

Current practice in the management of patients with type 2 diabetes mellitus in Saudi Arabia

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ABSTRACT

الأهداف: جمع البيانات عن الممارسات الحالية في علاج مرضى داء السكري النوع الثاني (T2DM) في المملكة العربية السعودية ولتقييم درجة الالتزام بالتعليمات الدولية.

الطريقة: تمثل هذه الورقة نتائج بيانات مرضى السكري من النوع الثاني T2DM السعوديين والتي تم جمعها في موجة 2006م من دراسة ممارسة إدارة مرض السكري الدولية (IDMPS). جمعت البيانات على شكل تقارير عن الحالات في الفترة مابين 2006/12/01 و 2006/12/30م. وتضمنت لمحة عن الحياة السكانية والاجتماعية والاقتصادية، علاج مرض السكر والسيطرة الأيضية.

النتائج: تمت دراسة 353 مريض مصاب بمرض السكري T2DM. كان متوسط العمر 51.61 ± 10.84 عام، وكان متوسط مدة الإصابة بمرض السكري 8.25 ± 6.49 عام. لم يتم عمل أي تقييم لاحتمال الإصابة بمضاعفات السكري أو عوامل الإصابة بأمراض القلب والشرايين أثناء السنة السابقة في 63-86%. تم علاج 7% من جميع مرضى للسكري من النوع الثاني T2DM بالأنسولين لوحده، و 28% بالحبوب الخافضة للسكر (OGLD) مع الأنسولين و 64% بالحبوب الخافضة للسكر OGLD لوحدها. وكان معدل HbA1c يقدر $8.20 \pm 1.89\%$ في جميع المرضى، ومن بين كل المرضى هناك 27% فقط وصل هدف HbA1c وهو أقل من 7%، بينما تمت السيطرة على نسبة السكر في الدم في 42% من المرضى عن طريق الأطباء. وصل الهدف المنشود لضغط الدم فقط في 16% $< 130/80$ و 65% كان لديهم مستوى الدهون فوق المستوى المثالي.

خاتمة: وجد أن غالبية المرضى لم تصل إلى الهدف الموصى به لتنظيم مستوى السكري مما يشير إلى وجود فجوة بين التوصيات أو التعليمات الدولية والممارسات الفعلية.

Objectives: To gather data on current practices in the management of patients with type 2 diabetes mellitus (T2DM) in Saudi Arabia and to evaluate the degree of compliance with international guidelines.

Methods: This paper represents the results of the Saudi Arabia T2DM data collected at the cross-sectional part of Wave 2006 of the International Diabetes Management Practices Study (IDMPS). Data were collected on a case report form from 28 health centers all over the Kingdom of Saudi Arabia, in the period between 01/12/2006 and 30/12/2006. It included demographic and socioeconomic profile in addition to diabetes management and metabolic control.

Results: Three hundred and fifty-three Saudi T2DM diabetic patients were studied. The mean age was 51.61 ± 10.84 years; average duration of diabetes was 8.25 ± 6.49 years; 63-86% had never been screened for diabetes complications or cardiovascular risk factors during the previous year. Of all patients with T2DM, 7% were treated with insulin alone, 28% with oral glucose lowering drug (OGLD) + insulin and 64% with OGLD alone. The average last hemoglobin A1c (HbA1c) was $8.20 \pm 1.89\%$ and among all patients, only 27% had reached the target HbA1c of $< 7\%$ while 42% of patients had been considered as reached glycemic control by physicians. Sixteen percent attained the target blood pressure of $< 130/80$, and 65% had lipid profile above the optimal level.

Conclusions: The majority of patients did not attain the recommended target glycemic level. This indicates the presence of a gap between recommendations of the international guidelines and the actual practices.

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The prevalence of diabetes mellitus (DM) in Saudi Arabia was found lately to be one of the highest around the world.¹ The explosive increase in the prevalence of diabetes and the consequences of its complications and associated disorders represents the greatest health care challenge facing the world today.² Moreover, the diabetic population consumes a disproportionate share of health care resources because of both microvascular and macrovascular complications. The Cost of Diabetes Type II in Europe (CODE-2) study estimated the total direct costs for 10 million people with type 2 diabetes in 8 participating European countries to be 29 billion Euros (US\$ 27 billion) in 1998.³ The same study also estimated that 3 times the healthcare resources are being spent on treating diabetes complications compared with that spent on controlling diabetes before the onset of complications. Therefore, the major goal of treatment of diabetic patients should be the achievement of an optimal (near normal) metabolic control, thus preventing the onset of the long-term complications. International diabetes societies such as the American Diabetes Association (ADA) have made global recommendations aiming at achieving optimal levels of glycemic control with hemoglobin A1c (HbA1c) of <7%.⁴ In addition, substantial efforts are devoted to improve physician compliance with evidence-based guidelines. Despite all recommendations, a large number of patients are not well-controlled, and do not reach the target metabolic control. Therefore, there is a need to better assess the current practices in diabetes management and put some actions into place in order to improve the quality of care for these patients. Epidemiological studies or national registers has been conducted at a country level or at regional levels, particularly in western countries, in order to assess the quality of care in diabetic patients, or to check compliance with national treatment guidelines and national programs for the improvement of quality of care of these patients.^{5,6} However, there is a lack of data on the quality of care of diabetic patients, particularly in type 2 patients, in several countries specifically, the non-Western countries.

This paper represents the results of the Saudi Arabia type 2 diabetes mellitus (T2DM) data collected at Wave 2 (2006) of the cross-sectional part of the International Diabetes Management Practices Study,⁷ which was carried out with an objective to evaluate the current practices in the management of patients with T2DM in Saudi Arabia and to evaluate the degree of compliance with international guidelines.

Methods. The International Diabetes Management Practices Study (IDMPS) is an international, multi-center, observational study of patients with DM.⁷ Its aim is to collect data in a standardized manner that

reflects current practices in the management of subjects with DM, in order to improve these practices over time. The primary objective is to assess the therapeutic management of T2DM in the current medical practice. Secondary objectives are: to study the proportion of patients reaching target metabolic control as per the international recommendations, and to evaluate the physician's perceptions of such control. The IDMPS was designed to continue for 5 years and to have 5 waves; the first wave started in 2005. The methodology has been described in detail by Chan et al⁷ who recently published the results of the Wave One study. The study design and reporting format are consistent with the recommended Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.⁸

Wave 2 (2006) of the cross-sectional study was carried out in 27 countries within Africa, Asia, Eastern Europe, the Middle East, and Latin America. This paper represents the results of the Saudi Arabia T2DM data collected during this wave. Data were collected by the treating physicians in case report form. Information regarding demographic and socioeconomic profile, self-monitoring of blood glucose (SMBG), access to diabetic educator, medical history, medications, hospitalizations, work absenteeism, and follow up were recorded. Measurement of height, weight, and waist circumference was carried out, and body mass index (BMI) was calculated using the formula: weight (kg)/height (m²). Outcome measure including attainments of target metabolic control defined as HbA1c <7%, low-density lipoprotein (LDL) cholesterol <100mg/dl, and blood pressure <130/80 mm Hg⁹ were documented. The study was supported by Sanofi-Avantis International and the implementation was coordinated by a steering committee that monitored the study progress and reviewed and validated the study documents. Report forms with deficient data were returned for completion.

Diabetologists, endocrinologists, and general practitioners expert in managing diabetic patients were invited to participate. The sample size was determined based on the assumption that insulin was the least prescribed therapy in terms of proportions. The sample size was determined in order to establish the frequency of insulin-treated patients. It was calculated to give an estimation of proportions with an absolute precision of 20% and a confidence interval (CI) of 95%. The number and profile of the physicians to participate in the study was determined based on the patients' sample size. Considering that each physician was requested to enroll 10 T2DM patients, the number of physicians was the number of patients divided by 10 and rounded off to the next digit. Exclusion criteria were recent commencement of insulin therapy, and active participation in another clinical trial.

In Saudi Arabia, it was planned to select 29 sites and to recruit 288 T2DM patients. Each physician enrolled at least the first 10 T2DM patients aged 18 years or older who attended their clinic over 2 weeks. A total of 28 physicians and 353 T2DM patients were actually recruited. A written informed consent was taken from all patients. The study was carried out in the period between 01/12/2006 and 30/12/2006. Data were collected from 28 health centers all over the Kingdom of Saudi Arabia. Approval was obtained from appropriate regulatory and ethics committee prior to the commencement of the study.

All data were transferred from Saudi Arabia to Mapi-Naxis, France, for quality control and analysis. All patients who satisfied the eligibility criteria of the cross-sectional study without missing data concerning the treatment of diabetes (patient currently receiving OGLD (yes/no) and currently insulin treated (yes/no), the status of metabolic control, and physician perception of metabolic control were analyzed in the whole population.

Descriptive analysis was performed. Qualitative data were summarized in frequency tables, and quantitative data were summarized in quantitative descriptive statistics. Fisher's exact tests and χ^2 test were used as appropriate. A *p*-value of <0.05 with 95% CI was considered to be significant. Statistical analyses were conducted with the SAS Software (version 8.02; SAS Institute, Cary, NC) Software AdClin 2.3 was used to format tables and listings.

Results. A total of 353 T2DM subjects were enrolled in the study. Table 1 shows some of the baseline characteristics of these subjects. The mean age is around 50 years. Males have non-significant lower BMI (*p*>0.05) and waist circumference (*p*>0.05) compared to females. The mean disease duration was 8.25±6.49 years and the mean last HbA1c carried out was 8.20 ± 1.89. 84% are "Arab, Oriental, or Persian", and 70% had a positive family history of diabetes. Of the 353 patients, 88% had health coverage, whether public or private. Only 45% had been educated by diabetes educators and very few (6%) were members of diabetes associations, 22% were literate. Sixteen percent of patients are smokers and another 16% were past smokers.

Figure 1 shows that considerable proportions of T2DM patients had never been screened in the previous one year for diabetes complications and or cardiovascular risk factors. Only 20% were screened for cardio vascular diseases while only 14% of patients had their lipids profile measured. Evolution for diabetic foot ulcers was carried out more frequently than evaluation for nephropathy or retinopathy. Approximately 35.4% of T2DM patients had been on insulin, either alone

or in combination with oral glycemia lowering drugs (OGLDs); 92.3% were on OGLDs either alone or in combination with insulin, and very few patients (<1%) were on diet and exercise alone (Figure 2). Seventy-two percent of T2DM patients treated with insulin alone had been on premix insulin, and none had been on basal insulin. Whereas, 46% of patients treated with OGLDs + insulin had been on premix insulin alone,

Table 1 - Baseline characteristics of T2DM subjects.

Baseline characteristics	Enrolled subjects
Age (years)	51.61 ± 10.84
Body mass index (kg/m ²): male	29.23 ± 4.29
Body mass index (kg/m ²): female	32.28 ± 5.74
Waist circumference (cm) : male	102.85 ± 15.25
Waist circumference (cm) : female	103.67 ± 16.20
Time since diagnosis (years)	8.25 ± 6.49
Last HbA1c (%)	8.20 ± 1.89

Data are means ± SD. T2DM - type 2 diabetes mellitus, HbA1C - hemoglobin A1c

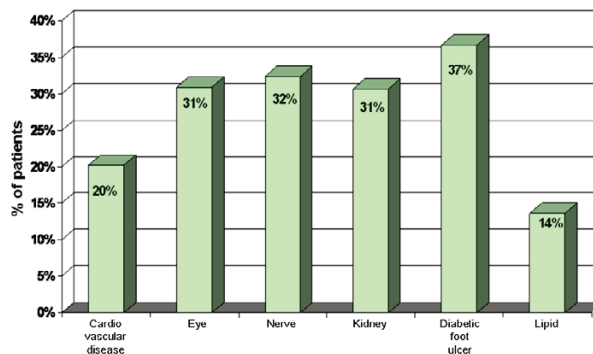


Figure 1 - Screening for diabetes complications and/or cardiovascular risk factors in the previous 12 months.

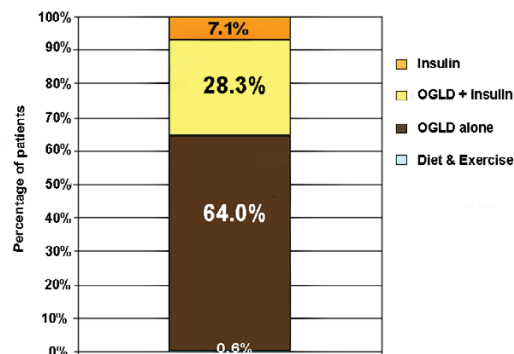


Figure 2 - Treatment map of patients. OGLD - oral glucose lowering drugs.

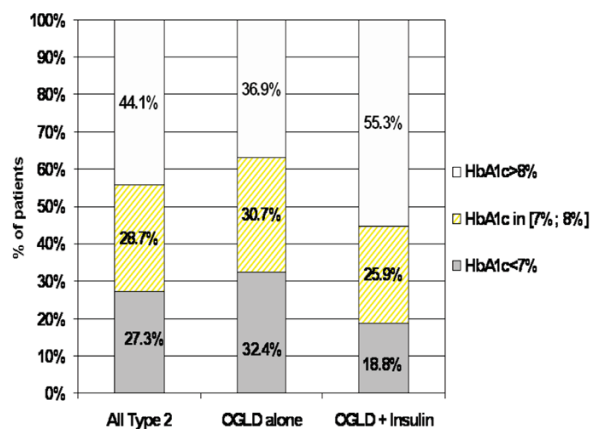


Figure 3 - Patients reached hemoglobin A1c (HbA1c) target treated with either OGLDs alone or with insulin. OGLD - oral glucose lowering drugs.

Table 2 - Dosages of insulin and percentages of patients reaching hemoglobin A1c goal in oral glucose lowering drugs (OGLDs) + insulin and insulin alone regimens.

Dosages of insulin	Total number of patients	Number at goal (%)	Total dose (IU/Kg) mean±SD
<i>OGLDs + insulin (n=100)</i>			
Basal only	41	8 (20.0)	0.28 ± 0.13
Premix only	46	2 (4.3)	0.70 ± 0.28
<i>Insulin alone (n=25)</i>			
Basal only	0	0 (0)	0
Premix only	18	3 (16.7)	0.81 ± 0.31

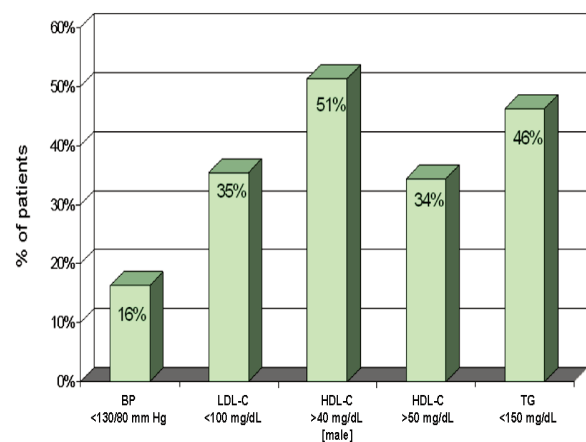


Figure 4 - Control of cardiovascular risk factors. BP - blood pressure, LDL-c - low density lipoprotein-cholesterol, HDL-c - high density lipoprotein-cholesterol, TG - triglyceride

and 41% had been on basal insulin alone. Patients had been on insulin therapy for only 1-3.5 years while the median duration of diabetes was 5-10 years. Fifty-one percent of T2DM patients treated with OGLDs + insulin self monitor their fasting blood glucose in a frequency of 10 times/month (median), while 30% of patients treated with OGLDs alone self monitor their fasting blood glucose at a frequency of 10 times/month. In addition, 81% of patients had HbA1c testing carried out within the last 6 months and 19% of patients had HbA1c tested less frequently. Less than one third of all patients with T2DM had reached a target HbA1c of <7%. The target HbA1c was reached by 32% of patients treated with OGLDs alone, while only 19% of patients treated with OGLDs + insulin reached the target (Figure 3). With regard to T2DM patients treated either with OGLDs + insulin or insulin alone, Table 2 shows that very few patients reached the HbA1c target using basal insulin or premixed insulin, while the mean dose of basal insulin is much lower than the dose of the premixed insulin. Where data on both the clinical judgment and laboratory HbA1c were available, we found that while 42% of patients were considered as reaching glycemic control by physicians, only 27% reached the HbA1c target of <7% in reality. Only 16% reached the target blood pressure of <130/80 mm Hg and 65% had LDL-C >100 mg/dl (Figure 4). Among the patients studied, 63% worked full time. Sick leave due to diabetes for an average of 5 days in the previous 3 months was reported by 28.7% of patients. Among the unemployed patients, disability to work was due to diabetes in 1.4%. Hospitalization due to diabetes in the previous 3 months amounted to 20.3% of T2DM patients.

Discussion. In this study, females were found to have non-significant higher BMI and higher mean waist circumference compared to male patients. Al-Nozha et al,¹ found the association between central obesity and DM to be more evident among Saudi female subjects. The high rate of a positive family history is consistent with the high prevalence of diabetes in the community. Despite of the fact that almost 90% of the patients have health care coverage, only 45% were evaluated by diabetic educators, keeping in mind the fact that only 22% of patients are literate. This indicates an underestimation of the importance of diabetes education by both the health providers and the patients. The IDF recommended in their global guidelines to ensure that education is accessible to all people with diabetes.⁹ Annual evaluation for complications and cardiovascular risk factors for an early detection and management is recommended by most of the diabetic societies including American Diabetes Association (ADA) and

International Diabetes Federation (IDF).^{4,9} Despite of all of these recommendations, considerable proportions (63-86%) of T2DM patients involved in this study had never been screened in the previous 12 months for one or more of the diabetes complications or cardiovascular risk factors. That adds more evidence to the need for implementing health education programs. Similar low rates of screening were also reported from other Arabian countries such as the United Arab Emirates (UAE)¹⁰ and Egypt.¹¹ This study did not determine the exact cause of non-adherence to the international guidelines as it did not test the compliance of patients to regular screening. Only 0.6% of patients were treated with lifestyle changes alone, which may implicate the lack of patient's adherence to such an important mode of therapy.¹² Most patients were treated with OGLDs, and approximately one third of patients were treated with insulin either alone or in combination with OGLDs despite of the fact that mostly of patients were uncontrolled. On the other hand, the median duration of insulin therapy was 1-3.5 years while the median duration of diabetes was 5-10 years supporting the evidence for clinical inertia.¹³ Despite of that the dose of basal insulin being lower than the dose of premixed insulin, a higher percentage of patients on basal insulin attained the target HbA1c. The most common insulin regimen in this study was the premix insulin, although basal insulin therapy was proven to be safer and more effective.^{14,15} This may reflect a bias of the treating physicians towards the use of premix insulin.¹⁶ Self monitoring of blood glucose is considered to be an important component of the standards of medical care in diabetes;⁴ however, the optimal frequency of SMBG in T2DM patient is not clear and many recent studies questioned the usefulness of SMBG in patients with T2DM, particularly those who are not using insulin.^{17,18} Around half of our patients treated with OGLDs + insulin self monitor their fasting blood glucose, while approximately one third of patients treated with OGLDs alone self-monitor their fasting blood glucose. In addition, more than 80% of patients had HbA1c carried out in the last 6 months, which is consistent with both the ADA and IDF recommendation,^{4,9} reflecting an easy access to health care. This is different from what was found by Chan et al⁷ who reported that 33% of their T2DM patients did not have health coverage, and 36% never had HbA1c measured. Although many of our patients had their HbA1c performed, most of patients were not in the glycemic targets, again supporting the issue of clinical inertia. The mean HbA1c was 8.20 ± 1.89 , which is similar to the HbA1c reported in another study on the quality of diabetes care in Saudi Arabia.¹⁹ Less than one third of patients attained the target HbA1c of <7%. The achievement of HbA1c target was higher among

patients treated with OGLDs alone than patient treated with OGLDs + insulin where very few patients reach HbA1c targets using basal or premix insulin. In their study, Chan et al⁷ found that the use of few OGLDs was a predictor of glycemic control. In addition to the poor glycemic control, only 16% and 35% attained the recommended target level of blood pressure and LDL. Similar findings was reported recently from Saudi Arabia,^{19,20} UAE,²¹ and internationally.²² Diabetic patients are at increased risk of developing cardiovascular disease and management of those patients should go beyond the glycemic control in order to improve their outcome.²³⁻²⁵ The lack of achievement of glycemic targets and the poor control of the cardiovascular risk factors is mostly related to therapeutic inertia rather than poor patient's compliance;²⁶ however, this point was not evaluated in our study. Smoking adds to cardiovascular risk. In this study, 16% are smokers and 16% were past smokers, compared to only 4.3% current smokers and 36.9% ex-smokers found in a recent cross sectional analysis from the UK,²⁷ again supporting the evidence for the need for diabetic education. Similar to what was reported by Chan et al,⁷ we found a mismatch between physicians' perception of patients' glycemic control and the actual HbA1c, which is an issue that should be explored to recognized the reason behind this mismatch. Irrespective of the reasons; updating the knowledge of the managing physicians with the international guidelines should be considered. The current study shows that 63% of patients worked full time. Sick leave due to diabetes for a mean of 5 days in the previous 3 months was reported among 28.7%, while hospitalization due to diabetes in the previous 3 months was 20.3% of T2DM patients. Disability to work was due to diabetes in 1.4% of unemployed patients. Keeping in mind the high prevalence of DM among the Saudi population, we think that the economic impact is huge. Data on resource consumption has been collected prospectively, and will allow in the future publications to analyze the economic impact of diabetes in Saudi Arabia.

This study has some limitations. Besides being a cross sectional study and the non-standardized laboratory assays, there is a lack of actual assessments of diabetic complications and a lack of evaluation of the barriers for not achieving glycemic or cardiovascular risk factor targets. In addition, the direct and indirect economic burden of diabetes was not calculated. Physician's knowledge of international guidelines is not explored and reasons behind the mismatch between their clinical judgment of patients' control and the laboratory HbA1c were not studied. Despite of the above limitations, our studies added to the previous evidence on the suboptimal metabolic control among Saudi diabetic patients.

In conclusion, this study confirms the gap between the practical guidelines for managing diabetic patients and the actual practice in Saudi Arabia. There is an urgent need for education of both patients and health care providers aiming for better glycemic control and therefore to slow down or prevent the development of all diabetes-related complications with its economic consequences.

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References

- Al-Nozha MM, Al-Maatouq MA, Al-Mazrou YY, Al-Harathi SS, Arafah MR, Khalil MZ et al. Diabetes Mellitus in Saudi Arabia. *Saudi Med J* 2004; 25: 1603-1610.
- Zimmer P, Alberti KG, Shaw J. Global and societal implications of the diabetes epidemic. *Nature* 2001; 414: 782-787.
- Nassu-Benedetti M. CODE-2 Advisory Board. The cost of diabetes Type II in Europe: the CODE-2 Study. *Diabetologia* 2002; 45: S1-S4.
- American Diabetes Association. Standards of Medical care in Diabetes-2009. *Diabetes Care* 2009; 32: S13-S61.
- Mottur-Pilson C, Snow V, Bartlett K. Physician explanations for failing to comply with "best practices." *Eff Clin Pract* 2001; 4: 207-213.
- Tan KB. Assessing doctors' compliance with guidelines on diabetes management. *Int J Health Care Qual Assur Inc Leadersh Health Serv* 2006; 19: 267-286.
- Chan JC, Gagliardino JJ, Baik SH, Chantelot JM, Ferreira SR, Hancu N, et al. Multifaceted determinants for achieving glycemic control: the International Diabetes Management Practice Study (IDMPS). *Diabetes Care* 2009; 32: 227-233.
- Von Elm E, Altman DG, Egger M, Pocock SJ, Gotsche PC, Vandenbroucke JP, et al. The Strengthening of the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet* 2007; 370: 1453-1457.
- IDF Clinical Guidelines Task Force. Global Guideline for Type 2 Diabetes: Recommendations for standard, comprehensive, and minimal care. *Diabet Med* 2006; 23: 579-593.
- Afandi B, Ahmad S, Saadi H, Elkhumaidi S, Karkoukli MA, Kelly B, et al. Audit of a diabetes clinic at Tawam Hospital, United Arab Emirates, 2004-2005. *Ann N Y Acad Sci* 2006; 1084: 319-324.
- Youssef AA, El Mahalli AA, Akl OA, Zaghoul AA. Quality of diabetes care in primary care setting in Egypt and example of health sector reform in developing countries. *J Egypt Public Health Assoc* 2006; 81: 301-320.
- Ripsin CM, Kang H, Urban RJ. Management of Blood Glucose in Type 2 Diabetes Mellitus. *Am Fam Physician* 2009; 79: 29-36.
- Hsu WC. Consequences of delaying progression to optimal therapy in patients with type 2 diabetes not achieving glycemic goals. *South Med* 2009; 102: 67-76.
- Janka HU, Plewe G, Riddle MC, Kliebe-Frisch C, Schweitzer MA, Yki-Järvinen H. Comparison of basal insulin added to oral agents versus twice-daily pre-mixed insulin as initial insulin therapy for type 2 diabetes. *Diabetes Care* 2005; 28: 254-259.
- Barnett A, Begg A, Dyson P, Feher M, Hamilton S, Munro N. Insulin for type 2 diabetes: choosing a second-line insulin regimen. *Int J Clin Pract* 2008; 62: 1647-1653.
- DeWitt DR, Hirsch IB. Outpatient insulin therapy in type I and type 2 diabetes mellitus: scientific review. *JAMA* 2003; 289: 2254-2264.
- Farmer A, Wade A, Goyder E, Yudkin P, French D, Craven A, et al. Impact of self monitoring of blood glucose in the management of patients with non-insulin treated diabetes: open parallel group randomized trial. *BMJ* 2007; 335: 132-139.
- O'Kane MJ, Bunting B, Copeland M, Coates VE, ESMON study group. Efficacy of self monitoring of blood glucose in patients with newly diagnosed type 2 diabetes (ESMON study): randomized controlled trial. *BMJ* 2008; 336: 1174-1177.
- Eledrisi M, Alhaj B, Rehmani R, Alotaibi M, Mustafa M, Akbar D, et al. Quality of diabetes care in Saudi Arabia. *Diabetes Res Clin Pract* 2007; 78: 145-146.
- Azab AS. Glycemic control among diabetic patients. *Saudi Med J* 2001; 22: 407-409.
- Saadi H, Carruthers SG, Nagelkerke N, Al Maskari F, Afandi B, Reed R, et al. Prevalence of diabetes mellitus and its complications in a population-based sample in Al Ain, United Arab Emirates. *Diabetes Res Clin Pract* 2007; 78: 369-377.
- Steinberg BA, Bhatt DL, Mehta S, Poole-Wilson PA, O'Hagan P, Montalescot G et al. Nine-year trends in achievement of risk factor goals in the US and European outpatients with cardiovascular disease. *Am Heart J* 2008; 15: 719-727.
- Milicevic Z, Raz I, Beattie SD, Campaigne BN, Sarwat S, Gromniak E, et al. Natural history of cardiovascular disease in patients with diabetes: role of hyperglycemia. *Diabetes Care* 2008; 2 (Suppl 31): S155-S160.
- Stolar MW, Hoogwer BJ, Gorshow SM, Boyle PJ, Wales DO. Managing type 2 diabetes: going beyond glycemic control. *J Manag Care* 2008; Pharm 14 Suppl B: S2-S19.
- Kong AP, Yang X, Ko GT, So WY, Chan WB, Ma RC, et al. Effects of treatment targets on subsequent cardiovascular events in Chinese patients with type 2 diabetes. *Diabetes Care* 2007; 30: 953-959.
- Schmittiel JA, Uratsu CS, Karter AJ, Heisier M, Subramanian U, Mangione CM et al. Why don't diabetes patients achieve recommended risk factor targets? Poor adherence versus lack of treatment intensification. *J Gen Intern Med* 2008; 23: 588-594.
- Bulugahapitiya U, Siyambalapatiya S, Sithole J, Fernando D, Idris I. Coexistence of smoking and metabolic syndrome among middle-aged patients with diabetes in the UK: a cross-sectional analysis. *Diab Vasc Dis Res* 2007; 4: 241-242.