

**Cardiovascular risk factors in Saudi Arabian and non-Saudi Arabian diabetic patients in Saudi Arabia**

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عوامل الاختطار القلبية الوعائية في السكرى من السعوديين وغيرهم في المملكة العربية السعودية  
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الخلاصة: لدراسة تواتر عوامل الاختطار القلبية الوعائية في السكرى من السعوديين وغير السعوديين، قُمتُ بدراسة المرضى الذين راجعوا مستشفى جامعة الملك عبد العزيز للمتابعة في الفترة بين كانون الثاني/يناير 1997 وكانون الأول/ديسمبر 2001 ودرست عوامل الاختطار القلبية الوعائية التي تشمل فرط ضغط الدم وفرط شحيمات الدم والسمنة والتدخين إلى جانب درجة السيطرة على سكر الدم. وقد بلغ عدد المرضى المدروسين 1122 مريضاً منهم 48% من السعوديين و52% من غير السعوديين، ولم تلاحظ فروق يُعتدُّ بها إحصائياً في معدلات انتشار عوامل الاختطار القلبية الوعائية بين السعوديين وغير السعوديين، وقد أوضحت دراسة الترابط بين كل عامل من عوامل الاختطار وعمر المريض ترابطاً يُعتدُّ به مع كل من فرط الدم والتدخين.

**ABSTRACT** To determine frequency of cardiovascular risk factors in Saudi and non-Saudi diabetics, we studied patients attending King Abdulaziz University Hospital for follow-up in the period January 1997 to December 2001. Cardiovascular risk factors, including hypertension, hyperlipidaemia, obesity and smoking, were studied as well as degree of blood glucose control. Of 1122 patients in the study, 48% were Saudis and 52% non-Saudis. No statistically significant difference was found for prevalence of cardiovascular risk factors between the two groups. Correlation of each of the risk factors to patient's age showed significant correlation to hypertension and smoking.

**Les facteurs de risque cardio-vasculaire chez des patients diabétiques saoudiens et non saoudiens en Arabie saoudite**

**RESUME** Afin de déterminer la fréquence des facteurs de risque cardio-vasculaire chez des diabétiques saoudiens et non saoudiens, nous avons étudié les patients qui sont venus à l'Hôpital universitaire King Abdulaziz en consultation de suivi durant la période janvier 1997-décembre 2001. Les facteurs de risque cardio-vasculaire, comprenant l'hypertension, l'hyperlipidémie, l'obésité et le tabagisme, ainsi que le degré de contrôle de la glycémie, ont été étudiés. Parmi les 1122 patients de l'étude, 48 % étaient des Saoudiens et 52 % des non-Saoudiens. Aucune différence statistiquement significative n'a été constatée entre les deux groupes pour la prévalence des facteurs de risque cardio-vasculaire. La corrélation de chacun des facteurs de risque à l'âge du patient montrait une corrélation significative avec l'hypertension et le tabagisme.

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## Introduction

Cardiovascular disease (CVD) is the leading cause of morbidity and death [1,2]. Diabetes mellitus (DM) is closely associated with ischaemic heart disease and patients with DM and no previous history of ischaemic heart disease have the same risk for cardiac events as patients with previous myocardial infarction [3,4]. This fact led the American national cholesterol education programme to state that, in terms of cardiovascular risk, DM was equivalent to having ischaemic heart disease [3]. People with diabetes have a 2-4 fold increase in the risk of dying from the complications of CVD [5]. Hyperlipidaemia, hypertension, smoking and obesity are well known, modifiable, cardiovascular risk factors in both diabetics and non-diabetics [6-10]. Rith-Najarian et al. have reported regional variation in CVD risk factors among American Indians and Alaskan natives with DM [11]. We aim in our work to study the prevalence of CVD risk factors in diabetics in two different groups, Saudi Arabians and non-Saudi Arabians.

## Methods

The study was conducted at King Abdulaziz University Hospital, a teaching hospital in the Western Province of Saudi Arabia. Patients seen in our hospital include mainly Saudis as well as patients from neighbouring Asian and African countries. The study group comprised 1155 diabetic patients, all those attending the hospital for follow-up from January 1997 to December 2001. Thirty-three (3%) were excluded as some of their data were missing. The remaining 1122 were included in the study; 541 (48%) were Saudis, with male:female ratio of 1.3:1 and 581 were non-Saudis (52%), with male:female ratio 1.1:1 ( $P = 0.3$ ).

CVD risk factors included hypertension (patient previously diagnosed or has 2 consecutive readings  $> 130$  mm Hg systolic blood pressure, 85 mm Hg diastolic blood pressure), hyperlipidaemia (if the patient has been previously diagnosed or has low density lipoprotein  $> 2.6$  mmol/L, triglyceride  $> 2.3$  mmol/L, high density lipoprotein  $< 0.9$  mmol/L for males and 1.0 mmol/L for females), obesity (defined as body mass index (BMI)  $> 30$  kg/m<sup>2</sup>), smoking history (either active or less than 5 years since cessation of smoking) were recorded from the medical records of the study group. In addition, participant's age, sex, nationality, degree of blood glucose control (poor blood glucose control defined as mean of the two most recent HbA1c readings  $> 9\%$ ), type and duration of DM were also recorded. The study group was divided into 2 groups according to nationality, Saudi or non-Saudi, and a comparative analysis was done regarding the prevalence of CVD risk factors and degree of blood glucose control. The group was also analysed according to age group,  $< 45$  years or  $\geq 45$  years.

Statistical analysis was performed using SPSS software. Mean  $\pm$  standard deviation was determined for quantitative data, and frequency for categorical variables. Chi-squared was used to analyse group difference for categorical variables. For continuous variables, *t*-test was used when comparing two groups. Pearson correlation was used to study the correlation of different cardiovascular risk factors to age.  $P < 0.05$  was considered significant.

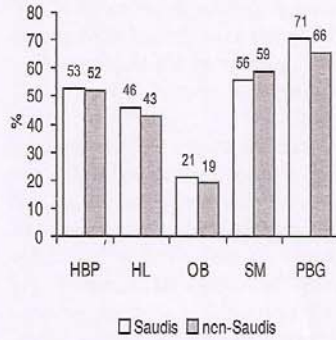
## Results

Type 2 diabetes was the most prevalent type recorded in both Saudis and non-Saudis, 454 of 541 (84%) and 471 of 581

(81%) respectively ( $P = 0.4$ ). Mean duration of diabetes was  $8.9 \pm 7.3$  years in Saudis versus  $8.8 \pm 7.2$  years in non-Saudis ( $P = 0.2$ ). There were 406 of 541 (75%) Saudis aged 45 years or over and 407 of 581 (70%) non-Saudis ( $P = 0.06$ ).

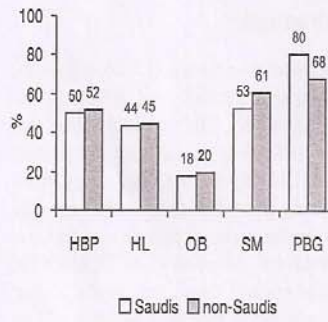
Hypertension, hyperlipidaemia, and smoking were common CVD risk factors in both Saudis and non-Saudis, while obesity was less common in both groups. Both groups had poor blood glucose control (Figure 1). There was no statistically significant difference in the prevalence of CVD risk factors in those above or below 45 years in both nationalities (Figures 2,3). Smoking was higher in young (<45 years) non-Saudis (61%) compared to those 45 years or over (58%) ( $P = 0.06$ ).

No significant difference in the frequency of cardiovascular risk factors in relation



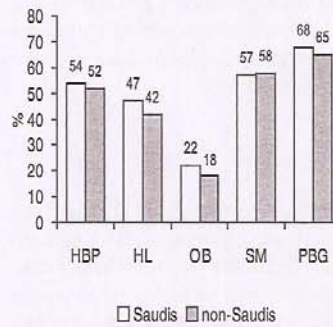
HBP = hypertension.  
HL = hyperlipidaemia.  
OB = obesity.  
SM = smoking.  
PBG = poor blood glucose control (HbA1c > 9%).  
P-value was significant for poor blood glucose control ( $P = 0.04$ ).

Figure 1 Comparison between Saudi ( $n = 541$ ) and non-Saudi ( $n = 581$ ) diabetics according to cardiovascular risk factors



HBP = hypertension.  
HL = hyperlipidemia.  
OB = obesity.  
SM = smoking.  
PBG = poor blood glucose control (HbA1c > 9%).  
P-value was significant for poor blood glucose control ( $P = 0.02$ ).

Figure 2 Cardiovascular risk factors among Saudi ( $n = 135$ ) and non-Saudi ( $n = 174$ ) diabetics < 45 years



HBP = hypertension.  
HL = hyperlipidaemia.  
OB = obesity.  
SM = smoking.  
PBG = poor blood glucose control (HbA1c > 9%).  
P-value was not significant ( $P = 0.3$ ).

Figure 3 Cardiovascular risk factors among Saudi ( $n = 406$ ) and non-Saudi ( $n = 407$ ) diabetics > 45 years

to age was found between Saudis and non-Saudis in 3 age groups (< 30 years, 30–60 years and > 60 years) (Table 1). Correlation of each of the risk factors to patient's age showed significant correlation to hypertension and smoking ( $P < 0.001$ ).

## Discussion

CVD complications are the leading cause of death and disability in people with diabetes. People with diabetes have significantly higher cardiovascular mortality rates compared to people without diabetes [12–14]. Age is considered a risk factor for CVD in people with diabetes [15]. Howard et al

[16] and others [17,18] have found that diabetes is the strongest CVD risk factor among individuals aged 45–74 years. The great majority of patients in our study, Saudis (70%) or non-Saudis (75%), were 45 years and over.

A large body of evidence from epidemiological, case-control, and cohort studies provides convincing documentation of the causal link between cigarette smoking and health risks [10]. Studies of individuals with diabetes consistently found a high risk of morbidity and premature death associated with the development of macrovascular complications among smokers [19]. Our study showed that, apart from poor control

Table 1. Prevalence of cardiovascular risk factors in Saudi and non-Saudi diabetics for three different age groups

Cardiovascular risk factor	Age group (years)	Patients having risk factor (%)		P
		Saudi	Non-Saudi	
Hypertension	<30	8	6	0.1
	30–60	39	38	
	>60	57	47	
Hyperlipidaemia	<30	34	32	0.4
	30–60	56	52	
	>60	52	58	
Obesity	<30	24	14	0.2
	30–60	40	39	
	>60	43	36	
Smoking	<30	26	33	0.2
	30–60	40	42	
	>60	51	53	
HbA1c > 9%	<30	4	6	0.9
	30–60	20	18	
	>60	6	8	

< 30 years, Saudis (n = 54) (10%), non-Saudis (n = 41) (7%).  
 30–60 years, Saudis (n = 281) (52%), non-Saudis (n = 366) (63%).  
 > 60 years Saudis (n = 206) (38%), non-Saudis (n = 174) (30%).

of blood glucose, smoking is the commonest CVD risk factor in both Saudis and non-Saudis, being commoner in non-Saudis. Similarly high smoking rates were reported by the Inter-Tribal Heart Study [20] and others [21,22]. Smoking cessation is one of the few interventions that can safely and cost-effectively be recommended for all patients [10]. It had been shown that smoking cessation counselling is effective in reducing tobacco use in this high-risk group [23,24].

Hypertension is a common problem in people with diabetes. Reported prevalence varies from 42% to 70% [11,25-27]. We report a rate of 52% and 53% in Saudis and non-Saudis respectively. Data from the recent United Kingdom Prospective Diabetes Study hypertension study [28,29] and the Hypertension Optimal Treatment trial [30] demonstrated that aggressive lowering of blood pressure was accompanied by reduction in macrovascular events.

People with diabetes exhibit increased rates of prevalence of lipid-rich atheroma and more thrombosis than non-diabetics [31,32]. These differences suggest a greater vulnerability for plaque rupture and coronary thrombosis in patients with DM [31-33]. Some of these abnormalities may be related to the dyslipidaemia associated with DM [32]. Almost half of the patients studied, both Saudis (46%) and non-Saudis (43%), have hyperlipidaemia, a finding in agreement with what has been reported by Howard et al [34] and others [11,17]. Recent studies have shown that CVD morbidity and mortality associated with DM can be considerably reduced through intensified treatment of hyperlipidaemia [35-37].

Obesity is a major modifiable risk factor for coronary heart disease along with cigarette smoking and elevated serum cholesterol [38]. The incidence of coronary heart disease events has been correlated to BMI

in a study of more than 23 000 employees in north-western Germany (PROCAM) [39]. This prospective study showed a rise in coronary events with increasing BMI over 8 years of follow-up from 31 events per 1000 at BMI < 20 kg/m<sup>2</sup> to 72 per 1000 at BMI > 30 kg/m<sup>2</sup>.

In Saudi Arabia, obesity and diabetes have become major causes of morbidity in big cities in the last 2 decades, apparently due to the sudden change in lifestyle as a result of economic development, urbanization and competitive lifestyles [40]. In a study conducted in Riyadh [41], obesity (BMI > 30 kg/m<sup>2</sup>) was reported in 33% of adult diabetics. Another study showed a figure of 27% in Bahrain [42]. In our study, overall around 20% of the patients were obese with no significant difference between Saudis and non-Saudis. These rates were much lower than those reported in some other countries where a rate around 50%-70% has been reported [11,17,22,43-45]. Obesity is multifactorial, not only environmental but also genetic factors contribute to its development [46]. It has been estimated that the heritability for BMI is over 30% and the rest is accounted for by other factors like demographic, familial and personal factors [46,47]. The lower prevalence of obesity in our study group (Saudis 21% and non-Saudis 19%) could be related to the nature of the local diet, but the effects this along with duration of residency of non-Saudis or the time of appearance of diabetes (after reaching Saudi Arabia or before) were not investigated in our study. Further studies are needed on the cause of this lower rate of obesity in people with diabetes in the Gulf region compared to other regions of the world.

Several studies have shown the health benefits of weight loss in people with diabetes; it improved glycaemic control [48], insulin sensitivity [49], triglyceride and

high density lipoprotein levels [50], and it also increases life expectancy [51].

It has been shown that greater degree of hyperglycaemia is associated with increasing CVD mortality in individuals with diabetes [52]. We report a high frequency of poor blood glucose control in both Saudis (71%) and non-Saudis (66%). Several studies clearly demonstrated that tight blood glucose control is important in delaying the onset and slowing the progression of microvascular complications [53,54].

Our study showed that CVD risk factors (smoking, hypertension, hyperlipidaemia and obesity) and poor glycaemic control are common in both Saudi and non-Saudi diabetics. Lifestyle may have a role; most of the patients are living a sedentary life, without much activity and using automobiles for travelling even very short distances.

Poor compliance of patients to medications, dietary restriction and follow-up may have an effect on the prevalence of CVD risk factors. Patients may get fed up taking chronic multiple medications and restrict-

ing their diet for a disease which is almost asymptomatic. Some patients may not be able to afford the medications, especially the new expensive generation, or may be ignorant due to lack of information.

Patient education regarding the diabetes disease process, nutritional management, physical activity, weight loss, cessation of smoking, compliance to medication and follow up, glucose monitoring, and prevention and detection of complications is of great importance. The success of diabetic teaching programmes seems to be similar in the inpatient and ambulatory settings. A study conducted by Muller and colleagues showed that people with diabetes who received identical education programmes in 2 different settings were no different in regard to improvement in HbA1c, BMI, hypoglycaemic episodes and subsequent hospitalization after one year [55]. Another important issue is physician education regarding screening for CVD risk factors and initiation of early and aggressive treatment when indicated.

### References

1. Tunstall-Pedoe H et al. Myocardial infarction and coronary deaths in the World Health Organization MONICA Project. Registration procedures, event rates, and case-fatality rates in 38 populations from 21 countries in four continents. *Circulation*, 1994, 90:583-612.
2. Hoyert D, Kochanek K, Murphy SL. Deaths: final data for 1997. *National vital statistics reports*, 1999.
3. Expert panel on detection, evaluation, and treatment of high blood cholesterol in adults. Executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert panel on
4. Haffner S et al. Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. *New England journal of medicine*, 1998, 4:229-34.
5. Malmberg K et al. Impact of diabetes on long-term prognosis in patients with unstable angina and non-Q-wave myocardial infarction: results of the OASIS

- (Organization to Assess Strategies for Ischemic Syndromes) Registry. *Circulation*, 2000, 102:1014-9.
6. Stein B et al. Influence of diabetes mellitus on early and late outcome after percutaneous transluminal coronary angioplasty. *Circulation*, 1995, 91:979-89.
  7. Egede L, Zheng D. Modifiable cardiovascular risk factors in adults with diabetes: prevalence and missed opportunities for physician counseling. *Archives of internal medicine*, 2002, 162(4):427-33.
  8. Yudkin JS. How can we best prolong life? Benefits of coronary risk factor reduction in non-diabetic and diabetic subjects. *British medical journal*, 1993, 306:1313-8.
  9. Halfiner SM. Obesity and the metabolic syndrome: the San Antonio Heart Study. *British journal of nutrition*, 2000, 83(suppl. 1):S67-70.
  10. Haire-Joshu D, Glasgow RE, Tibbs TL. Smoking and diabetes. *Diabetes care*, 2003, 26(suppl. 1):S89-90.
  11. Rith-Najarian S et al: Regional variation in cardiovascular disease risk factors among American Indians and Alaska Natives with diabetes. *Diabetes care*, 2002, 25(2):279-83.
  12. Roper N et al. Cause-specific mortality in a population with diabetes: South Tees Diabetes Mortality Study. *Diabetes care*, 2002, 25(1):43-8.
  13. de Marco R et al. Cause-specific mortality in type-2 diabetes. The Verona Diabetes Study. *Diabetes care*, 1999, 22: 756-61.
  14. Gu K, Cowie CC, Harris MI. Mortality in adults with and without diabetes in a national cohort of the U.S. population 1971-1993. *Diabetes care*, 1998, 21: 1138-45.
  15. American Diabetes Association. Aspirin therapy in diabetes. *Diabetes care*, 2002, 25(suppl. 1):S78-79.
  16. Howard BV et al. Coronary heart disease prevalence and its relation to risk factors in American Indians. The Strong Heart Study. *American journal of epidemiology*, 1995, 142:254-68.
  17. Welty TK et al. Cardiovascular disease risk factors in American Indians. The Strong Heart Study. *American journal of epidemiology*, 1995;142:269-87.
  18. Howard BV et al. Rising tide of cardiovascular disease in American Indians. The Strong Heart Study. *Circulation*, 1999, 99:2389-95.
  19. Haire-Joshu D, Glasgow RE, Tibbs TL. Smoking and diabetes (Technical review). *Diabetes care*, 1999, 22:1887-98.
  20. CDC Centers for Disease Control and Prevention: *Intertribal Heart Project: Results from the cardiovascular health survey*. Atlanta, Georgia, 1996.
  21. Mendlein JM et al. Risk factors for coronary heart disease among Navajo Indians: findings from the Navajo Health and Nutrition Survey. *Journal of nutrition*, 1997, 127(suppl. 10):2099S-105S.
  22. Howard BV. Risk factors for cardiovascular disease in individuals with diabetes. The Strong Heart Study. *Acta diabetologica*, 1996, 33:180-4.
  23. Counseling to prevent tobacco use. In: US Prevention Services Task Force. *Guide to clinical preventive services*, 2nd ed. Baltimore, Maryland, Williams & Wilkins, 1996:597-609.
  24. Fiore MC et al. *Smoking cessation*. Clinical Practice Guidelines No. 18. Rockville, Maryland, Agency for Health Care Policy and Research, 1996, Publication No. 96-0692.



25. Wokoma FS. Hypertension in non-insulin dependent diabetic Nigerians: a comparative analysis of normotensive and hypertensive subgroups. *Diabetes international*, 1999, 9:57-8.
26. Akbar D. Is hypertension common in hospitalized type-2 diabetic patients? *Saudi medical journal*, 2001, 2:139-41.
27. Haupt E et al. The KID Study VI: diabetic complications and associated disease in younger type 2 diabetics still performing a profession. Prevalence and correlation with duration of diabetic state, BMI, and C-peptide. *Experimental and clinical endocrinology & diabetes*, 1999, 7:435-41.
28. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. UK Prospective Diabetes Study Group. *British medical journal*, 1998, 317:703-13.
29. Efficacy of atenolol and captopril in reducing risk of macrovascular and microvascular complication in type-2 diabetes; UKPDS 39 UK Prospective Diabetes Study Group. *British medical journal*, 1998, 317:713-20.
30. Hansson L et al. Effect of intensive blood pressure lowering and low dose aspirin in patients with hypertension: principal results of the Hypertension Optimal Treatment (HOT) randomised trial. HOT Study Group. *Lancet*, 1998, 351:1755-62.
31. Moreno PR et al. Coronary composition and macrophage infiltration in atherectomy specimens from patients with diabetes mellitus. *Circulation*, 2000, 102:2180-4.
32. Papadakis JA et al. Treating dyslipidaemia in non-insulin-dependent diabetes mellitus - a special reference to statins. *Journal of diabetes and its complications*, 2001, 15:211-26.
33. Malmberg K et al. Impact of diabetes on long-term prognosis in patients with unstable angina and non-Q-wave myocardial infarction: results of the OASIS (Organization to assess strategies for ischemic syndromes) registry. *Circulation*, 2000, 102:1014-9.
34. Howard BV et al. Plasma and lipoprotein cholesterol and triglyceride concentrations in the Pima Indians: distributions differing from those of Caucasians. *Circulation*, 1983, 68:714-24.
35. Pyorala K et al. Cholesterol lowering with simvastatin improves prognosis of diabetic patients with coronary heart disease. A subgroup analysis of the Scandinavian Simvastatin Survival Study (4S). *Diabetes care*, 1997, 20:614-20.
36. Goldberg RB et al. Cardiovascular events and their reduction with pravastatin in diabetic and glucose intolerant myocardial infarction survivors with average cholesterol levels: subgroup analyses in the cholesterol and recurrent events (CARE) trial. The Care Investigators. *Circulation*, 1998, 98: 2513-9.
37. Prevention of cardiovascular events and death with pravastatin in patients with coronary heart disease and a broad range of initial cholesterol level. The Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID) Study Group. *New England journal of medicine*, 1998, 339:1349-57.
38. Eckel RH, Krauss RM. American Heart Association call to action: obesity as a major risk factor for coronary heart disease. AHA Nutrition Committee. *Circulation*, 1998, 97:2099-100.
39. Schulte H, Cullen P, Assmann G. Obesity, mortality and cardiovascular disease in the Münster Heart Study (PROCAM). *Atherosclerosis*. 1999, 144:199-209.

40. Seba ZA. *Health in Saudi Arabia*, 1st ed. Riyadh, Tihama Publications, 1985:16.
41. El Hazmi MA, Warsy AS. Prevalence of overweight and obesity in diabetic and non-diabetic Saudis. *Eastern Mediterranean health journal*, 2000, 6(2-3):276-82.
42. Zurba FI. Characteristics and pattern of care of diabetes in primary health care centres in Bahrain. *Bulletin of the Arab Group for Study of Diabetes*, 1994, 3(1): 9-18.
43. Denny CH, Holtzman D. *Health behaviors of American Indians and Alaska Natives: findings from the behavioral risk factor surveillance system, 1993-1996*. Atlanta, Georgia, Centers for Disease Control, 1999.
44. Williams G. Management of non-insulin-dependent diabetes mellitus. *Lancet*, 1994, 343:95-100.
45. Walia M et al. Prevalence of coronary risk factors in non-insulin dependent (type 2) diabetics. *Journal of the Association of Physicians of India*, 1999, 47(11):1051-5.
46. Bouchard C. Genetic aspects of human obesity. In: Bjorntorp P, Brodoff BN, eds. *Obesity*. Philadelphia, JB Lippincott, 1992:343-51.
47. Epstein FH, Higgin M. Epidemiology of obesity. In: Bjorntorp P, Brodoff BN, eds. *Obesity*. Philadelphia, JB Lippincott, 1992:330-42.
48. Goldstein DJ. Beneficial health effects of modest weight loss. *International journal of obesity and related metabolic disorders*, 1992, 16:397-415.
49. Friedman JE et al. Restoration of insulin responsiveness in skeletal muscles of morbidly obese patients after weight loss: effect on muscle glucose transport and glucose transporter GLUT4. *Journal of clinical investigation*, 1992, 89:701-5.
50. Wing RR et al. Long term effects of modest weight loss in type II diabetic patients. *Archives of internal medicine*, 1987, 147:1749-53.
51. Lean ME et al. Obesity, weight loss and prognosis in type 2 diabetes. *Diabetic medicine*, 1990, 7:228-33.
52. Sievers MI, Bennett PH, Nelson RG. Effect of glycemia on mortality in Pima Indians with type 2 diabetes. *Diabetes*, 1999, 48:896-902.
53. 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. *Lancet*, 1998, 352:837-53.
54. Ohkubo Y et al. Intensive insulin therapy prevents the progression of diabetic microvascular complications in Japanese patients with non-insulin-dependent diabetes mellitus: a randomized prospective 6-years study. *Diabetes research and clinical practice*, 1995, 28:103-17.
55. Muller UA et al. Should insulin therapy in type 2 diabetes be started on out- or in-patient basis? Results of a prospective controlled trial using the same treatment and teaching programme in ambulatory care and a university hospital. *Diabetes & metabolism*, 1998, 24:251-5.