

Effect of weight loss on cardiovascular risk factors among obese individuals in a weight management programme in Brunei Darussalam

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ABSTRACT

Introduction: The prevalence of obesity is escalating in Brunei Darussalam with a number of clinics and programme expanding to counteract this problem. Studies have showed that lifestyle intervention with weight loss reduces the risk of cardiovascular (CV) disease. The purpose of the study was to evaluate the outcomes of a Weight Management Programme (WMP), and to examine the correlation between weight change and changes in glycaemic control, blood pressure (BP) and lipid levels. **Materials and Methods:** A retrospective data collection from obese participants enrolled in a 24-week WMP in 2011. The multidisciplinary programme included educational group sessions, individual counseling and physical exercise classes. Body weight, fasting blood sugar (FBS), BP and lipid profile at baseline and 24-week were retrieved. **Results:** Obese participants (n=220) enrolled in the programme with 104 (47.3%) completed at 24-week. The mean weight lost was 5.35 kg (6.1%) ($p < 0.001$). Significant reduction in mean FBS (0.31 mmol/l, $p = 0.009$), diastolic BP (2.82 mmHg, $p = 0.012$), and triglyceride, 0.17 mmol/l ($p = 0.002$) and a significant increase in mean high density lipoprotein cholesterol, 0.04 mmol/l ($p = 0.016$) were observed at 24-week. No significant association was found between body weight loss and improvements in the cardiovascular risk factors. **Conclusions:** Participants who completed a 24-week WMP can significantly and clinically reduce body weight and improve a number of cardiovascular risk factors. The improvements in the risk factors, however, were not associated with the weight loss.

Keywords: Cardiovascular risk factors, diet, lifestyle programme, obesity, physical exercise, weight loss

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INTRODUCTION

Over the past decades, Brunei Darussalam has undergone dramatic changes in socio-economic growth and development. The changing lifestyle comes concurrently with

the emerging obesity pandemics. Preliminary data showed that the prevalence of obesity is increasing from 12% in 1996 to 27.2% in 2011.^{1, 2} Obesity has become a major public health concern, presenting a burden of non-communicable diseases including diabetes mellitus, hypertension, stroke, cardiovascular disease and cancer.³

In Brunei Darussalam a number of clinics and programme have been established to counteract this problem, primarily through healthy lifestyle intervention. Research studies on healthy lifestyle intervention with predominantly Caucasian study population often claim the beneficial effect of weight loss on cardiovascular risk factors. However analyses from these interventions do not always reveal consistent findings.

Results from a 24-week weight management programme (WMP) incorporating group-based educational session and individual counseling on diet, physical exercise and psychology reported a significant weight loss and improvement in fasting blood sugar (FBS), total cholesterol (TC), low density lipoprotein (LDL) cholesterol, high density lipoprotein (HDL) cholesterol and triglycerides (TG).⁴ The researchers, however, did not find any relationship between weight loss and changes in the cardiovascular risk factors except TG.⁴ A study on a 24-week weight loss programme reported a significant association between weight change and the changes in HbA_{1c} and SBP.⁵ In a randomised controlled trial of a 24-week behavioural lifestyle programme versus physical exercise programme, Blumenthal *et al.* reported a significant weight loss and improvement in FBS, SBP and DBP among their participants in the be-

havioural lifestyle programme.⁶ In another 24-week weight loss programme, the researchers reported a slight non-significant weight loss in the group receiving the n-3 polyunsaturated fatty acid (PUFA) supplement and placebo. Significant improvement was seen in HDL cholesterol and TG in the n-3 PUFA group, while the placebo group experienced significant improvement only in TG. No significant changes were reported on the other risk factors.⁷ In contrast, a study on a 24-week intervention programme found no significant improvement in SBP, DBP, TC, LDL cholesterol, HDL cholesterol and TG and no significant association was reported between body weight change and changes in the cardiovascular risk markers.⁸

Despite the growing number of evidence, research evaluating the effect of weight loss on cardiovascular risk factors is lacking in Brunei Darussalam. The aim of the present study was to provide primary evaluation on the outcomes of the effects of WMP in Brunei Darussalam and to examine the correlation between the magnitude of weight loss and the degree of improvement in glycaemic control, blood pressure and lipid levels.

MATERIALS AND METHODS

Study design and participants: A single-centered, retrospective cohort study using data of obese participants enrolled in a 24-week WMP in the year 2011. Participants entered the programme as walk-in or referred from healthcare centres or hospitals. In order to be eligible for the programme, participants were required to be older than 18 years of age, have a BMI ≥ 30 kg/m². They were not eligible to join the programme if they were pregnant, had a chronic inflammatory condi-

tion, liver disease or malignancy. We included data of all participants in the programme without inclusion or exclusion criteria or sampling.

Intervention: The purpose of the programme was to achieve 5-10% weight loss through lifestyle behaviour modifications focusing on reducing caloric intake and increasing physical activity, with an emphasis on sustainable behaviour change.

Prior to starting the programme, all participants were required to undergo a comprehensive medical assessment. Upon completion of the medical assessment, participants were invited to attend the first educational group session where they completed the demographic and health status questionnaires. A weekly educational and motivational group session was arranged for the first 9 weeks. Topics of the group sessions included healthy eating, physical activity, ways to overcome barriers to weight management, prevention of relapse, an educational visit to a supermarket and a healthy cooking demonstration. Immediately after every group session, participants were encouraged to participate in a 60-minute brisk walk around various recreational areas. In addition, a weekly aerobic session led by a fitness instructor was arranged for the first 10 weeks. The aerobic session provided moderate intensity physical activity lasting about 120 minutes per session. Individuals counseling sessions were fixed for all participants during the first 12 weeks of the programme. Each participant had a total of at least 5 individual counseling sessions with a medical officer, dietitians and an exercise physiologist. A clinical psychologist provided counseling sessions to a selected number of participants

based on the psychologist's assessment. Participants were instructed to record their food intake in a food diary. The dietitian reviewed the food diary and advised a healthy reduced calorie diet with an emphasis on reducing fat intake, increasing dietary fibre, modifying portion size of foods and sustainable dietary habits. An exercise physiologist prescribed individualised cardiovascular and resistance training programme with a target of 30 to 60 minutes of cardiovascular exercise 4 to 6 days per week.

Measures: All participants were scheduled to attend baseline and 24-week assessment, at which time anthropometric and laboratory measures were collected.

Anthropometric measures: The measurement of anthropometric data was performed by trained nurses of the WMP. Weight was measured to the nearest 10gm using a digital weighing scale (Seca 200 weighing scale, USA) with participants wearing no shoes. Height was measured to the nearest 0.5cm using a wall-mounted stadiometre. Seated blood pressure was measured after a 5-min rest using an automated device.

Laboratory measures: Blood samples were obtained after a fast of at least 8 hours. The fasting blood samples were collected in a hospital or healthcare centres. FBS, serum TC, LDL cholesterol, HDL cholesterol and TG were analysed in an accredited hospital-based laboratory.

Statistical analysis: Prior to statistical analysis, normality and distribution of all variables was examined. Independent *t* tests were used to compare continuous variables while the chi-

-square tests for categorical data. The primary analysis in the study was to examine the outcomes of a WMP. Paired *t* test was used to compare differences of mean values between baseline and 24-week for anthropometric and laboratory measures. Further analysis examined the correlation between weight loss and improvement in the cardiovascular risk factors. Spearman correlation coefficients were calculated to measure the strength and direction of potential relationship between percentage of weight change and changes in cardiovascular risk factors. All analyses were two-sided. Statistical analysis was performed using SPSS version 20.0.⁹

RESULTS

Table 1 presents the baseline characteristics of 220 obese individuals who were eligible to join the WMP in 2011. Majority (76.4%) of

the participants were women. The mean age 35.3 (8.64) years and weighed 91.4 (17.61) kg with a mean BMI of 37.1 (5.75) kg/m² at baseline. Thirty one (14%) of participants reported history of diabetes. Based on laboratory measures 11.4% had diabetes, 38.6% had hypertension and 51.4% had hyperlipidaemia.

One hundred and four (47.3%) participants returned at 24-week (completers) while 116 participants dropped out of the programme (non-completers). A comparison of completers and non-completers at baseline showed that non-completers had a significantly higher mean BMI ($p=0.012$) and had a greater proportion of participants with diabetes ($p=0.006$) compared to completers. No other significant difference between completers and non-completers was found.

There was significant reduction in body

Table 1: Demographic and clinical characteristics of participants at baseline.

	Overall participants <i>n</i> =220	Completers <i>n</i> =104	Non-completers <i>n</i> =116	<i>p</i> value †
Age in years	35.3 (8.64)	35.8 (8.82)	34.8 (8.48)	0.345
Males, <i>n</i> (%)	52 (23.6)	19 (18.3)	33 (28.5)	0.076
Weight in kg	91.4 (17.61)	87.1 (14.35)	95.3 (19.32)	<0.001
Height in m	1.57 (0.08)	1.55 (0.07)	1.58 (0.08)	0.003
BMI in kg/m ²	37.1 (5.75)	36.1 (4.45)	38.0 (6.60)	0.012
Self-reported DM	31 (14.1)	11 (10.6)	20 (17.2)	0.345
Diabetes ^a	25 (11.4)	8 (7.8)	17 (14.7)	0.006
Hypertension ^b	85 (38.6)	37 (35.6)	48 (41.4)	0.378
Hyperlipidaemia ^c	113 (51.4)	56 (53.8)	57 (49.1)	0.053
FBS, mmol/l	5.37 (2.05)	5.17 (1.56)	5.57 (2.42)	0.163
SBP, mmHg	126 (14.7)	125 (15.57)	127 (13.94)	0.345
DBP, mmHg	81.7 (10.7)	81.3 (10.98)	82.1 (10.37)	0.598
TC, mmol/l	5.21 (1.05)	5.14 (0.91)	5.28 (1.17)	0.353
LDL-C, mmol/l	3.43 (0.98)	3.38 (0.77)	3.48 (1.15)	0.437
HDL-C mmol/l	1.13 (0.21)	1.16 (0.21)	1.11 (0.20)	0.089
TG, mmol/l	1.49 (0.93)	1.45 (1.01)	1.53 (0.85)	0.527

† Chi-square and Independent t test were used to compare categorical and continuous data between completers and non-completers respectively.

^aWHO 1999 Global Guideline for Type 2 Diabetes¹⁰, Diabetes; ≥ 7.0 mmol/l, ^bHypertension; systolic blood pressure (BP) ≥ 140 mmHg or diastolic BP ≥ 90 mmHg (≥ 130 or ≥ 80 for diabetes). ^cHyperlipidaemia; total cholesterol (TC) >5.0 mmol/l. BMI = Body Mass Index.

Percentage (%) Change

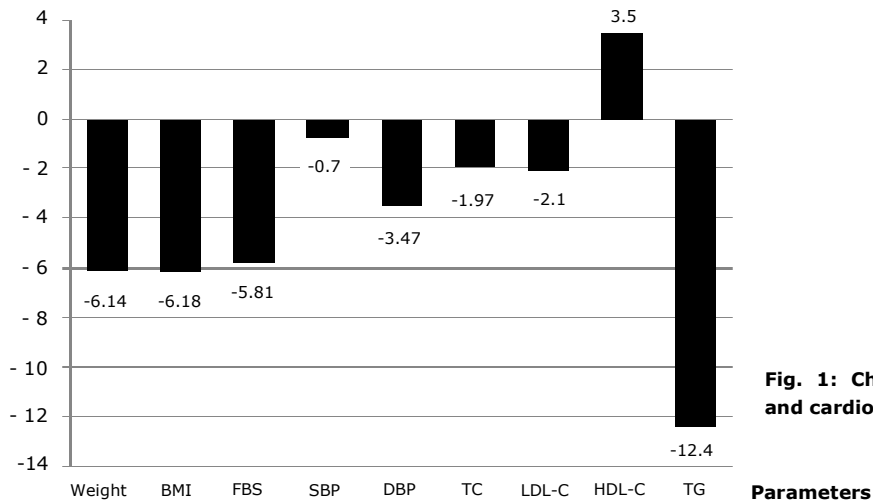


Fig. 1: Change in body weight and cardiovascular risk factors.

weight at 24 weeks ($p < 0.001$). The mean weight lost was 5.35 (0.47) kg or 6.14% of participants' initial body weight. Fifty-five percent of the participants lost at least 5% of their initial body weight.

There were significant improvements in a number of cardiovascular risk markers. FBS significantly reduced by 5.81% ($p = 0.009$), DBP significantly reduced by 3.47% ($p = 0.012$), HDL cholesterol signifi-

cantly increased by 3.50% ($p = 0.016$) while TG significantly reduced by 12.4% ($p = 0.002$) (Figure 1). There were slight improvements in SBP, TC and LDL cholesterol however these improvements did not reach statistical significance (Table 2).

There was no significant correlation between percentage of weight change and changes in any of the cardiovascular risk markers. The observed correlation coefficients

Table 2: Anthropometric measures and cardiovascular risk factors at baseline and 24 weeks.

	<i>n</i>	Baseline mean (SD)	24-week mean (SD)	Mean change (95% CI)	Change (%)	t stats (df)	<i>p</i> value †
Weight (kg)	104	87.1 (14.4)	81.8 (14.4)	-5.35 (-6.3, -4.4)	-6.14%	-11.4(103)	<0.001
BMI (kg/m ²)	104	36.1 (4.45)	33.9 (4.47)	-2.23 (-2.6, -1.9)	-6.18%	-11.6 (103)	<0.001
FBS (mmol/l)	89	5.34 (1.69)	5.04 (1.70)	-0.31 (-0.5, -0.1)	-5.81%	-2.7 (88)	0.009
SBP (mmHg)	104	124.9 (15.1)	124.1 (14.2)	-0.88 (-3.6, 1.8)	-0.70%	-0.6 (103)	0.522
DBP (mmHg)	104	81.2 (11.1)	78.4 (9.71)	-2.82 (-5.0, -0.7)	-3.47%	-2.6 (103)	0.012
Total cholesterol (mmol/l)	85	5.07 (0.79)	4.97 (0.77)	-0.10 (-0.2, 0.02)	-1.97%	-1.7 (84)	0.099
LDL cholesterol (mmol/l)	86	3.33 (0.68)	3.26 (0.69)	-0.07 (-0.2, 0.04)	-2.10%	-1.3 (85)	0.197
HDL cholesterol (mmol/l)	86	1.14 (0.19)	1.17 (0.19)	+ 0.04 (0.01, 0.1)	+3.50%	2.5 (85)	0.016
Triglycerides (mmol/l)	85	1.37 (0.63)	1.21 (0.46)	-0.17 (-0.3, -0.1)	-12.4%	-3.2 (84)	0.002

† Paired t test was used to compare anthropometric and laboratory data between baseline and 24-week. The comparisons were performed only on those with both pre- and post-measures.

Table 3: Correlation between percentage of weight change and changes in the cardiovascular risk factors.

	Mean change at 24-week (SD)	Spearman correlation coefficient† (r)	<i>p</i> value
FBS (mmol/l)	-0.31 (1.09)	0.129	0.291
SBP (mmHg)	-0.88 (13.9)	-0.011	0.912
DBP (mmHg)	-2.82 (11.2)	0.055	0.590
Total chol (mmol/l)	-0.10 (0.58)	0.149	0.230
LDL chol (mmol/l)	-0.07 (0.51)	0.040	0.747
HDL chol (mmol/l)	+0.04 (0.13)	0.127	0.305
TG (mmol/l)	-0.17 (0.49)	0.154	0.212

(*r*) of all markers were graded as little or no correlation.

DISCUSSION

The goal of our study is to evaluate the effects of a WMP and examine the correlation between the magnitude of weight loss and degree of changes in cardiovascular risk factors. The mean percentage of weight loss in our programme achieved a statistical and clinical significance with 55% of our participants managed to achieve the target 5-10% weight loss. We acknowledge that the target weight loss does appear to be small and insignificant; however numerous studies and institutions including the Institute of Medicine, the National Institutes of Health and the National Heart, Lung and Blood Institute have established and advocated the beneficial effects of the modest weight loss.¹¹⁻¹³

Notably, the weight lost in our study is greater than that reported in other interventions that have focused exclusively on physical exercise alone.^{6, 8} The improvement in glycaemic control is consistent with previous studies that employed a group-based 24-week lifestyle modification programme.⁴⁻⁷ However, there was a slight variation in the

results. Different level of intensity allocated to different component in the programme appeared to have contributed to this effect. While previous studies provided verbal encouragement to increase physical activity, our programme provided a structured group exercise classes. This is in agreement with a recent meta-analysis that reported changes in HbA_{1c} was strongly associated with structured exercise training, not with physical activity advice alone.¹⁴ The marked improvement in DBP in our study is comparable to the previous studies.⁵⁻⁷ Unfortunately the improvement in SBP was small and did not correlate well with the previous studies. This could be attributable to the fact that our participants entered the programme with small elevation of SBP.

Similar to the previous studies participants in our programme experienced significant improvement in the HDL cholesterol and TG level.^{4, 7} However, the improvements in TC and LDL cholesterol in our study did not reach statistical significance. The explanations for the disparity are not immediately apparent. However, it is possible that our programme did not sufficiently address the dietary component to ameliorate the lipid pro-

files. Furthermore unlike a hospital-based intervention, ⁴ our participants with hyperlipidaemia may have not received aggressive management of hyperlipidaemia. Our programme is based in a Health Promotion Centre where new cases of hyperlipidaemia were referred to the participants' respective clinics. Unfortunately it is not known how many of these participants actually seek further medical attention. Other parameters that may have contributed to the variations in TC and LDL cholesterol response to the programme, including age, smoking status and baseline TC and LDL cholesterol level. Further research is needed to elucidate reasons for this disparity. Nevertheless, our study highlights the need of our programme to be constantly and systematically evaluated and improved. Based on the results, we have recommended an introduction of an educational group session in our programme focusing on dietary modification to alleviate lipid level. Our participants with hyperlipidaemia also need to be identified and followed-up in individual counseling for lipid-lowering dietary management.

The evidence for the association between body weight loss and changes in the cardiovascular risk factors is inconsistent. The results in our study add the weight to this evidence. Interestingly, despite the significant improvements of the risk factors in our study, there was little or no indication that the improvements were parallel with the participants' weight loss. It suggests that at 24-week the clinical improvements occurred independent of body weight lost and therefore may have been caused by other important factors, possibly by a more relevant component in the programme such as the dietary modification and/or the increase in physical

activity level. A review on the relationship between physical exercise and metabolic abnormalities reported that regardless of body weight loss, an increased level of physical exercise improves health outcomes. ¹⁵

It is also possible that our study duration is not long enough to allow a greater impact of the weight loss on the cardiovascular risk factors. A study documented that at 1 year body weight lost was significantly associated with many of the cardiovascular risk factors. ¹⁶ Another plausible explanation is that the change in body weight is not a responsive marker of the cardiovascular disease risks considering it does not take into account the changes that occur in the body compositions. Alternatively waist circumference has been increasingly used as an indicator of body fat distribution and regarded as a stronger predictor of cardiovascular disease outcomes, above and beyond the measurement of body mass index. ¹⁷⁻²⁰ Further research with a longer study duration is needed to establish the relationship between body weight loss and changes in the cardiovascular risk factors.

In interpreting our findings, several important limitations need to be considered. The large percentage of participants with diabetes that dropped out of our programme means that impact of the programme to the body weight and the risk factors is potentially enhanced. Like many of the previous studies, our results were not based on intention-to-treat analysis. Excluding those who had not completed the programme would have resulted in different outcomes. In keeping with the objectives of our study, we focused on body weight and cardiovascular risk markers in-

cluding lipid profile as the parameters and the follow-up at 24-week as the endpoint of our data collection. It should be noted that an abnormal lipid level alone does not reveal a complete picture of cardiovascular disease risk. Increasingly, the importance of qualitative abnormalities in the lipid profile, such as smaller, denser, and more easily oxidizable LDL particles and higher LDL apoB levels, is being recognized, even when TC and sub-fractions are normal.^{21,22} In addition, body weight regain following an active phase of weight loss is very common. Twenty-four weeks follow-up may not have been long enough to determine the clinical importance of a WMP. For this reason, we have initiated follow-up at 12-month aimed to provide support mechanism for weight maintenance and to collect anthropometric and laboratory data. In addition as part of our measures to reduce the attrition rate, a research study to identify factors that can be used as predictors of attrition is currently being proposed.

Given the clinical benefits of our programme and the escalating prevalence of obesity, public health recommendations for weight management in clinical settings such as clinics and health centres should integrate the establishment of a multidisciplinary programme that put emphasis on educational group sessions and physical exercise classes. Essentially such programme should incorporate the establishment of a database and implementation of a closed-loop continuous improvement model where ongoing effort should be undertaken to improve the quality of services, effectiveness and cost-effectiveness of the programme. The feasibility of implementing the basic structure of our programme in non-clinical settings such as schools and

workplaces is yet to be explored.

In conclusion, the findings in our study support the significance and effectiveness of a WMP that focused on group-based educational approach and structured physical exercise classes. Participants who completed the 24-week WMP can achieve a clinical and statistical significant weight loss and improvements in a number of cardiovascular risk factors. The improvements in the risk factors, however, were not associated with the body weight loss. Further research to evaluate and determine the effect of weight loss on the cardiovascular risk factors is warranted.

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REFERENCES

- 1:** National Nutritional Status Survey, Ministry of Health, Brunei Darussalam: 1996.
- 2:** National Health and Nutritional Status Survey, Ministry of Health, Brunei Darussalam: 2011.
- 3:** Must A, Spadano J, Coakley EH, Field AE, Colditz G, Dietz WH. The disease burden associate with overweight and obesity. *JAMA.* 1999; 282:1523-29.
- 4:** Graffagnino CL, Falko JM, Londe M, et al. Effect of a community-based weight management program on weight loss and cardiovascular disease risk factors. *Obesity.* 2005; 14:280-8.
- 5:** Dasgupta K, Hajna S, Joseph L, et al. Effects of meal preparation training on body weight, glycaemia, and blood pressure: results of a phase 2 trial in type 2 diabetes. *Intern J Behav Nutr and Phy Activ.* 2012; 9:125.
- 6:** Blumenthal JA, Sherwood A, Gullette ED, et al. Exercise and weight loss reduce blood pressure in

men and women with mild hypertension: *Arch Intern Med.* 2000; 160:1947-58.

7: Krebs JD, Browning LM, McLean NK, et al. Additive benefits of long-chain n-3 polyunsaturated fatty acids and weight-loss in the management of cardiovascular disease risk in overweight hyperinsulinaemic women. *Int J Obes.* 2006; 30:1535-44.

8: Arsenault BJ, Côté M, Cartier A, et al. Effect of exercise training on cardiometabolic risk markers among sedentary, but metabolically healthy overweight or obese postmenopausal women with elevated blood pressure. *Atherosclerosis.* 2009; 207:530.

9: IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.

10: World Health Organization. Definition, Diagnosis and Classification of Diabetes Mellitus and its Complications. Report of a WHO Consultation. Part 1: Diagnosis and Classification of Diabetes Mellitus. Geneva: WHO Department of Non-communicable Disease Surveillance. 1999:1-59.

11: Munro BH. *Statistic methods for health care research* (4th edition). Lippincott William & Wilkins: New York; 2000.

12: Umpierre D, Ribeiro PA, Kramer CK, et al. Physical activity advice only or structured exercise training and association with HbA_{1c} levels in type 2 diabetes: a systematic review and meta-analysis. *JAMA.* 2011; 305:1790-9.

13: Carroll S. and Dudfield M. What is the relationship between exercise and metabolic abnormalities? A review of the metabolic syndrome. *Sports Med.* 2004; 34:371-418.

14: Wing RR, Lang W, Wadden TA, et al. Benefits of modest weight loss in improving cardiovascular risk factors in overweight and obese individuals with type 2 diabetes. *Diabetes Care.* 2011; 34:1481-6.

15: Lean ME, Han TS, Morrison CE. Waist circumference as a measure for indicating need for weight management. *BMJ.* 1995; 311:158-61.

16: Janssen I, Katzmarzyk PT, Ross R. Waist circumference and not body mass index explains obesity-related health risk. *Am J Clin Nutr.* 2004; 79:379-84.

17: Haffner SM, Despres J-P, Balkau B, et al. Waist circumference and body mass index are both independently associated with cardiovascular disease: The International Day for the Evaluation of Abdominal Obesity (IDEA) survey. *J Am Coll Cardiol.* 2006; 47:358A.

18: Klein S, Allison DB, Heymsfield SB, et al. Waist circumference and cardiometabolic risk: a consensus statement from Shaping America's Health: Association for Weight Management and Obesity Prevention; NAASO, The Obesity Society; the American Society for Nutrition; and the American Diabetes Association. *Am J Clin Nutr.* 2007; 85:1197-202.

19: Barakat HA, Carpenter JW, McLendon VD, et al. Influence of obesity, impaired glucose tolerance and NIDDM on LDL structure and composition: possible link between hyperinsulinemia and atherosclerosis. *Diabetes.* 1990; 39:1527-33.

20: Stewart MW, Laker MF, Dyer RG, et al. Lipoprotein compositional abnormalities and insulin resistance in type II diabetic patients with mild hyperlipidemia. *Arterioscler Thromb.* 1993; 13:1046-52.