Adolescent Obesity in Kuwait:
Consequences and Treatment

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Abstract

Background: Obesity is a global problem that resulted from excessive positive energy balance. Decreased physical activity and other dietary, environmental and genetic factors all contribute to its development (Han et al., 2010). On a larger scope, social, economic and cultural factors also predisposed to its occurrence globally (WHO, 2000). Of particular concern is the rise in paediatric obesity with subsequent rise in morbidity during childhood, adolescence and young adulthood, and rise in morbidity in adulthood, including adult obesity, as well as increased risk of premature mortality in adulthood (Reilly and Kelly, 2011, Reilly, 2006).

In Kuwait, paediatric obesity prevalence is high and may be continuing to rise in all age groups (Mirmiran et al., 2010, Al-Isa and Thalib, 2008, Al-Isa and Thalib, 2006). Affluence and rapid transformation of Kuwaiti society after the discovery of oil is one theory behind the changes that took place in the dietary and physical activity patterns which could be the main mediators for the obesity epidemic in Kuwait (Ng et al., 2011). However, despite the paediatric obesity problem in Kuwait there is not a widely available treatment solution or attempts to find obesity treatment solutions locally (Al-Isa et al., 2010b). At an international level, effective treatment strategies were traditionally confined to the Western world, particularly the Epstein group in the USA (Epstein et al., 2012, Oude Luttikhuis et al., 2009, Epstein, 1996), though other successful treatment programmes have been published since the early pioneering work of Epstein (Ho et al., 2012).

The aim of the thesis was to: a) test the hypothesis that obesity impairs health related quality of life in Kuwaiti adolescents and test the differences in health related quality of life assessed by self-report and parent-proxy report, b) determine the prevalence of cardiometabolic risk factor abnormalities and metabolic syndrome in a sample of obese Kuwaiti adolescents, and c) test the effectiveness of a treatment intervention for adolescent obesity and compare it to a primary care control.

Methodology: Chapter 4 describes the health related quality of life study (HRQL) that was conducted at baseline comparing the HRQL between obese and healthy-weight Kuwaiti adolescents (aged 10 to 14 years). Five hundred eligible consenting participants were assessed using the Peds QL™ self-reports as well as 374 parent-proxy reports. From the

obese group (n= 224), 82 participants agreed to participate in the National Adolescent Treatment Trial for obesity (NATTO) (chapter 6), an assessor-blinded randomised controlled trial, and were randomised to the intervention programme or primary care control over 6 months. The intervention programme aimed to change sedentary behaviour, diet and physical activity in low intensity doses through 6 hours contact over 24 weeks. At baseline, 80 blood samples were collected from 80 out of the 82 participants from the NATTO study, for the assessment of cardiometabolic risk factors namely C-reactive protein, intracellular adhesion molecules, interleukin-6, fasting blood glucose, fasting insulin, alanine aminotransferase, aspartate aminotransferase, gamma glutamyltransferase, total cholesterol, low-density lipoprotein, high-density lipoprotein, triglycerides, and adiponectin. Metabolic syndrome was assessed using two criteria modified for use in younger individuals.

Results: From the health related quality of life study, obesity was not associated with impaired health related quality of life in regression analysis. In a structured paired comparison of 98 pairs of obese adolescents vs healthy weight peers, impaired health related quality of life reached significance only for the physical quality of life domain (obese group score = 87.5, healthy weight group score = 93.7, 95% CI for quality of life score = -1.5, -9.4, p 0.007). In a paired comparison between parent-proxy vs self-reports for the obese adolescents, physical quality of life score (parent-proxy score 81.3, self-report score 87.5, 95% CI = -3.2, -11.0, $p < 0.001$), psychosocial score (parent-proxy score 76.7, self-report score 85.0, 95% CI = -4.2, -10.8, $p < 0.001$) and total score (parent-proxy score 78.8, self-report score 84.8, 95% CI = -4.9, -10.9, $p < 0.001$) were all significantly lower in the parent reports. The cardiometabolic risk factors with highest prevalence of abnormal values in the sample (n = 80), described in chapter 5, were; aspartate aminotransferase (89% of samples abnormal), insulin resistance by homeostasis model assessment (HOMA) (67% abnormal), intracellular adhesion molecule (ICAM) (67% abnormal), fasting insulin (43.5%), C-reactive protein (42.5%), low density lipoprotein (LDL) (35%), total cholesterol (34% abnormal), and systolic blood pressure (30% abnormal). Of all participants (n=80), 77 had at least one impaired cardiometabolic risk factor besides their obesity. Prevalence of Metabolic syndrome was 21.3% using the International Diabetes Federation definition and 30% using the Third Adult Treatment Panel definition. At 6 months outcome in the treatment intervention NATTO, the trial had acceptable retention (n =31 from the intervention group and n =32 from the control group), but engagement with both the intervention and control treatment (as measured by

attendance at treatment sessions) was poor. The intervention had no significant effect on BMI Z score relative to control, and no other significant effects of the intervention were observed.

Conclusion: In a sample of obese Kuwaiti adolescents, obesity was not associated with marked impairment of health related quality of life; however, marked impairment in multiple cardiometabolic risk factors was present. Conducting the National Adolescent Treatment Trial for Obesity in Kuwait was feasible but not efficacious, and future obesity treatment trials should incorporate a qualitative assessment for better participants' engagement.

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To my loving parents

Love you forever and always

Author’s Declaration

‘I declare that, except where explicit reference is made to the contribution of others, that this dissertation is the result of my own work and has not been submitted for any other degree at the University of Glasgow or any other institution

Signature

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List of Abbreviations

ATP III	National cholesterol education programme adult treatment panel III
ALT	Alanine transanimase
AOM	America on the move trial
AST	Aspartate transanimase
ACVD	Atherosclerotic cardiovascular disease
BMI	Body Mass Index
BMI Z score	Body mass index Z score
BCT	Behaviour change therapy
CRP	C reactive protein
CDC	Center for disease control
CT scan	Computed tomography scan
CBC	Complete blood count
CI	Confidence interval
CONSORT	Consolidated standards for reporting trials
CHD	Coronary heart disease
CALO-RE	Coventry Aberdeen London-Revised taxonomy
DEXA	Dual-energy x-ray absorptiometry
ECI	Enhanced child involvement
ELISA	Enzyme-linked immunosorbent assay
EDTA	Ethylenediaminetetraacetic acid
EGIR	European group for the study of insulin resistance
FGIR	Fasting glucose and insulin ratio
FTO	Fat mass and obesity-associated gene
FAO	Food and agriculture organisation
FDA	Food and drug administration
FNA	Food and nutrition administration
FFAs	Free fatty acids
FBG	Fasting blood glucose
gGT	gamma glutamyl transferase
GDP	Gross domestic product
HRQL	Health related quality of life
HDL	High density lipoprotein
HOMA-IR	Homeostatic model assessment of insulin resistance
ITT	Intention to treat analysis
ICAM	Intercellular Adhesion molecule
IL-6	Interleukin 6
IDF	International diabetes federation
IOTF	International Obesity Task Force
IPEG	International paediatric endosurgery group
IQR	Interquartile range
KNSS	Kuwait national surveillance system
LDL	Low density lipoprotein
MRI	Magnetic resonance imaging

MS	Metabolic syndrome
mmHg	Millimeter of mercury
MOE	Ministry of education
MOP	Ministry of planning
NATTO	National adolescent treatment trial for obesity
NCHS	National centre for health statistics
NHMRC	National health and medical research council for Australia
NHBPEP	National high blood pressure education programme
NICE	National institute for health and care excellence
NAFLD	Non-alcoholic fatty liver disease
NASH	Non-alcoholic steatohepatitis
Peds QL™4.0	Pediatric quality of life generic questionnaire
PCOS	Polycystic ovarian syndrome
PSMF	Protein-sparing modified fast
PACI	Public authority for civil information
QUICKI	Quantitative insulin sensitivity check index
RCT	Randomised controlled trial
RFT	Renal function test
SCOTT	Scottish childhood obesity treatment trial
SIGN	Scottish intercollegiate guidelines network
SMS	Short message service
SNP	Single nucleotide polymorphism
SCOUT	Sirbutamine cardiovascular outcome trial
SES	Socioeconomic status
SD	Standard deviation
TG	Triglycerides
TNF-α	Tumour necrosis factor
UK	United Kingdom
UNICEF	United Nations International Children's Emergency Fund
VCAM	Vascular cell adhesion molecule
VLDL	Very low density lipoprotein
VLED	Very low energy diet
WHO	World Health Organisation

1. Introduction and Literature Review

1.1 Introduction

This chapter is a literature review of obesity, with particular interest in childhood and adolescent obesity, its definition, prevalence and trends, aetiology, consequences, prevention and treatment options. An overview of Kuwait and paediatric obesity prevalence in the country is also discussed.

1.2 Paediatric obesity: Definition

Defining paediatric obesity is of great clinical importance to ensure accurate diagnosis and to provide the appropriate treatment option. It is also of great epidemiological importance, in order to monitor prevalence and trends within and/ or in between populations.

Obesity is a chronic disease characterised by excess body fat which was included in the International Classification of Disease in 1948 (Duncan et al., 2010). It affects adults and children, populations of the developed and developing worlds, and is an ever growing public health concern worldwide. It has reached epidemic proportions, in 2010; overweight children under the age of 5 were estimated to be over 42 million, globally (WHO, 2012).

There are direct non-reference methods to measure body fat content such as dual-energy x-ray absorptiometry (DEXA), computer tomography (CT scans), magnetic resonance imaging (MRI), and bioelectrical impedance. These methods are usually informative, highly sensitive and specific, and reliable in terms of assessing true body fatness (Reilly et al., 2007). Mostly these methods are either expensive, labour intensive or not readily accessible in routine practice. Therefore, simpler and more practical proxy measurements of excess body fat are necessary for clinical as well as epidemiological purposes. In practice, different definitions exist for paediatric obesity using different methods of assessment such as waist circumference, percentage of ideal weight for height, weight for height Z scores, BMI percentiles and BMI Z score. These methods use either national or international reference data. Most of the reference data used, either nationally or internationally, are arbitrary and do not really reflect true correlation of specific cut off points with morbidity or mortality risk (Han et al., 2010). Body mass index (BMI) is a simple proxy of body fatness which can be obtained by the formula (weight kg/height^2 m^2).

For adults, internationally agreed cut off points for BMI define underweight (<18.5), normal weight (18.6-24.9), overweight (25-29.9) and obese (≥30). These cut off points correlate well with the risk of morbidity and mortality in adults (WHO, 2000).

On the other hand, definition of paediatric obesity is more complex and still lacks generalisability. Effects of age, gender, ethnicity, and puberty on growth makes classification of paediatric obesity difficult (Reilly, 2006). Definition of a standard age-related gender-specific growth charts with clinically significant reference points for overweight and obesity is of great public health importance to enable monitoring trends in paediatric obesity in the population and comparison with other populations internationally in terms of prevalence and /or trial outcomes.

However, Reilly (2006) argues, in the case of BMI for age, that a unique cut off point for increased BMI for age would not suffice to detect the point of increased morbidity in paediatric populations due to the fact that these obesity-associated comorbidities are many and involve multiple body systems, but any method used for the definition has to be sensitive (identifying those who are excessively fat) and specific (identifying those who are not excessively fat).

Gender-specific BMI for age percentile based on national representative data has been popular in use in the clinical and epidemiological settings (Reilly et al., 2010). In the UK, for example, the 1990 population-specific BMI percentile charts are used to define obesity at BMI $\geq 98^{th}$ percentile and overweight at BMI $\geq 91^{th}$ percentile (Rudolf et al., 2000). Also waist circumference for age, and BMI for age using internationally defined reference data have been in use widely clinically or in research. The latter was developed by the International Obesity Task Force (IOTF) Childhood obesity Working Group and published in 2000 where BMI percentiles involved combining data for children and adolescents aged 2 to 18 years from six large nationally representative samples from Brazil, United Kingdom, Hong Kong, the Netherlands, Singapore and the United States (Cole et al., 2000). Cole et al. (2000) developed the cut off points for overweight and obesity based on extrapolated adult cut off points at BMI ≥25 and BMI ≥30, respectively. One question remains however about the most appropriate method to be used when defining paediatric obesity.

This problem can be overcome, as Reilly et al (2010) explained in his systematic review by considering the accuracy of simple clinical and epidemiological definitions of childhood obesity. Firstly, using BMI for age with national reference data assured far more sensitivity and specificity in general and in between genders than using the IOTF percentiles with the international reference data. This is of great clinical importance in order to offer treatment to those who really suffer from health-threatening body fat content. Secondly, for the diagnosis of obesity with related cardiometabolic risk factors, high BMI for age with national reference data was as accurate a definition as the waist circumference for age method (Reilly et al., 2010).

Defining paediatric obesity raises another issue of defining change of weight status or body fatness over time and assessing the best estimate for fat mass change in response to weight management. Ideally, the method used here should aim to evaluate the percentage of body fat loss (Hunt et al., 2007). In 2005, Cole et al. conducted an observational study on a sample of 135 children aged 2 to 5 years over a period of 9 months. The aim was to detect the best measure of adiposity change in these children from BMI, BMI%, BMI Z score, or BMI percentile. They have concluded that BMI is a better method to detect adiposity change over time (Cole et al., 2005). Hunt et al (2007) pointed out that this study, being observational in nature detected reproducibility of the methods tested rather than a true fat mass reduction over the 9 month period. Hunt et al. (2007) had tested the use of BMI Z score, BMI, weight, and weight Z score to detect fat mass change against actual fat mass measurement by Tanita Bioimpedance segmental body composition analyser. The study sample was of 92 children (aged 7 to 19 years) attending a weight management clinic over a period of 12 months. Anthropometric and bioimpedance measurements were made 3 monthly. Hunt et al. (2007) found that BMI Z score was a better measure to predict change in fat mass over the other methods. Using bioelectrical impedance as the reference method to detect fat mass change limited the study results for being less accurate in detecting the body's fat mass and differentiating subcutaneous mass from visceral mass. However, to detect variation in body composition, a combination of bioelectrical impedance and anthropometry could be of great benefit in clinical settings (Wright et al., 2008).

In summary, BMI can be used as a tool to define obesity, and in paediatric populations, national or international age and gender specific BMI percentiles is considered a preferable tool to define paediatric obesity, if available. Monitoring fat mass change over time in paediatric population is best obtained by calculating BMI Z score at the start and end

points. Adding other tools to define obesity, anthropometric or direct non reference methods, could be of great value to detect variations of body composition.

1.3 Paediatric obesity prevalence and trends

1.3.1 Prevalence and trends – Kuwait

Back in 1979-1980 a joint FAO/UNICEF mission visited the Gulf countries in order to make a first assessment of the food and nutrition situation, with particular reference to infant and young children, hence the development of a nutrition survey (Musaiger, 1985). In 1994 the Kuwait Nutritional Surveillance System (KNSS) was developed in collaboration with the WHO as part of the Global Database on Child Growth and Malnutrition. The data used were of Kuwaiti infants who had completed one year of age. It used anthropometric cut off points of the WHO then, where for adolescents (10 to 19 years) overweight was defined as BMI $\geq 85^{th}$ age and sex specific percentile and for obesity using both BMI $\geq 95^{th}$ percentile and triceps skinfold thickness $\geq 90^{th}$ percentile, from the US National Centre for Health Statistics/World Health Organization growth reference (1 to 24 years)(WHO, 1995). It is based on health clinics distributed all over the 6 Kuwaiti governorates and selecting nationally representative samples by multistage random sampling methods. Data on weight, height, age and sex are collected and used to calculate levels of stunting, wasting, and obesity for the Kuwaiti population. Nutrition Surveillance is a system for consistent monitoring of the nutritional status of the population and its associated health, economic, demographic and food related variables. It is an instructive system that provides governments, on regular basis, with updated data on the nutrition status of their countries. It enhances the observation of nutrition-related risk factors and helps with the development of nutrition policy of the country (Butte et al., 2007).

The 1995 output of that surveillance showed that Kuwait was among the countries with the highest prevalence of overweight in all age groups (de Onis and Blossner, 2000). Yearly reports were sent to the Ministry of Health officials and to the WHO.

At an academic level within Kuwait, several studies have been conducted by members of the Faculty of Medicine to determine the prevalence of adolescent obesity and develop body mass index reference data for Kuwaiti children and adolescents (El-Bayoumy et al., 2009, Al-Isa and Thalib, 2008, Al-Isa and Thalib, 2006, Al-Isa, 2004). While prevalence of obesity in adolescence was remarkably high, the rate was relatively stable in studies done

on males and females aged 10 to 14 years in the year 2000 (14.7% and 13.1% respectively, obesity defined as BMI≥95th centile according to CDC reference charts) (Al Isa, 2004), and the year 2006 (14.6% and 14.2%, respectively, obesity defined as BMI ≥95th centile according to CDC reference charts) (El-Bayoumy et al., 2009). On the other hand, the comparison of BMI for age data for adolescent girls among three Middle Eastern countries (Egypt, Kuwait, Lebanon) showed that the highest rates of overweight and obesity were among the Kuwaiti girls (Jackson et al., 2007). Al Isa & Thalib (2006, 2008) collected anthropometric data for children aged 3-9 years old and adolescents aged 10-14 years old in Kuwait. Attempts were made to include all healthy, Kuwaiti kindergarten, elementary and intermediate school students. The aim was to establish population specific BMI reference data for Kuwaiti nationals and other regional countries. When compared with the United States National Centre for Health Statistics reference, the curves were similar except at the lowest percentile (5th) and higher percentiles (50th percentile onwards). The probable reason behind the incompatibility is that these surveys were done after the obesity epidemic hit Kuwait, suggesting that the national reference data might have been 'contaminated' by the obesity epidemic resulting in markedly higher BMI for age than those obtained using US CDC reference data (El-Ghaziri et al., 2011).

In 2007, the Kuwait nutritional surveillance system (KNSS) had adapted the reformed WHO international growth reference (de Onis et al., 2012), now called WHO child growth standards, for assessing overweight and obesity. These are merged data from the 1977 National Centre for Health Statistics (NCHS)/WHO growth reference (1-24 years) and BMI for age growth charts designed from the WHO growth standards for 2 to 5 year old children, that collected reference data from Brazil, Ghana, India, Norway, Oman and USA, and the BMI cut offs for adults. These new BMI for age percentiles provide fitting BMI for age reference for 5 to 19 years old children and adolescents. Here obesity is defined using BMI for age ≥ +2SD corresponding to BMI =30 for adults and overweight ≥ +1SD corresponding to BMI = 25 for adults. Table 1.1 displays the percentages of overweight and obesity in Kuwaiti male and female adolescents (aged 10 to 18) from the year 1996 to 2010, extracted from records of the KNSS-Ministry of Health-Kuwait.

Prevalence of adolescent obesity in the Arabian Gulf region is among the highest in the world (Ng et al., 2011).

Table 1.1 Kuwait Nutritional Surveillance System (KNSS)

Annual reports 1996-2010						
Year	Sample size	Age (y)	Overweight males (%)	Overweight females (%)	Obese males (%)	Obese females (%)
1996/97	10893	10 - 14	36.8	35.9	NA	NA
	10512	14 - 18	27.6	31.1	NA	NA
2001	3228	10 - 14	19.4	23.0	19.6	17.3
	3292	14 - 20	20.9	23.0	24.6	16.2
2002	2557	10 - 14	24.2	23.7	20.9	17.2
	2819	14 - 20	17.7	24.0	22.4	19.5
2003	1870	10 - 14	21.7	24.9	19.6	14.3
	3077	14 - 20	18.2	25.3	23.6	16.6
2004	2000	10 - 13	22.7	22.5	16.8	17.7
	2953	14 - 20	20.2	24.0	23.7	18.6
2005	1908	10 - 13	20.8	27.2	19.4	16.8
	3240	14 - 20	18.8	25.3	24.8	20.0
2006	2002	10 - 13	21.8	27.1	22.5	20.1
	2923	14 - 20	23.5	21.2	23.3	17.3
2007	1970	10 - 13	25.1	23.0	20.4	16.6
	3095	14 - 20	20.4	23.7	25.6	20.5
2008	1986	10 - 13	23.2	20.1	24.0	25.2
	3569	14 - 20	20.1	25.6	24.8	20.3
2009	1949	10 - 13	24.3	25.7	23.7	21.7
	3252	14 - 20	19.9	24.1	25.7	19.4
2010	3639	10 - 13	23.2	27.5	21.9	21.5
	4207	14 - 20	21.3	25.0	26.4	17.1

From 1996 to 2006 overweight was defined as BMI ≥ 85th age and sex specific percentile, and obesity defined using both BMI ≥ 85th age and sex specific percentile and skinfold thickness ≥ 90th percentile from the National Centre for Health Statistics/WHO reference data (WHO, 1995). From 2007 onwards overweight was defined as BMI ≥1SD corresponding to BMI = 25 in adults and obesity was defined as BMI ≥2 SD corresponding to BMI = 30 in adults, all based on the reformed WHO child growth standards for age and sex (de Onis et al., 2012).

Prevalence of adolescent (age 12 to 18 years) obesity from a nationally representative sample in the Kingdom of Saudi Arabia was 12.7% in 1998 (El-Hazmi and Warsy, 2002). In 2008, from a sample representing 3% of the population, the prevalence of adolescent obesity (age 15 to 18 years) was 33.1% (Bader et al., 2008). The prevalence of adolescent obesity in UAE in 2005 was 24.2% (Al Matroushi and Fikry, 2005) and in Qatar in 2004 the prevalence of adolescent obesity was 11% (Bener and Kamal, 2005). Although comparison is difficult to be made between all Arabian Gulf countries as different paediatric obesity definitions have been used (Ng et al., 2011), the prevalence in this region is among the highest in the world where Kuwait takes the lead.

In summary, studies and national surveillance efforts show that in Kuwait obesity among adolescents is high and levels of overweight and obesity in that age group had stabilised between surveys up until the last available survey of year 2010 (Mirmiran et al., 2010). From the Arabian Gulf region, prevalence of adolescent obesity is high and the highest is in Kuwait.

1.3.2 Prevalence and trends of paediatric obesity – Worldwide

Regardless of the definition used, it is now evident that the prevalence of childhood and adolescent obesity has increased dramatically over the last 3 decades in both the developing and developed worlds (Alwan, 2011), but might have been stabilising in the last few years in the western world (Rokholm et al., 2010). In the European region, studies show that the prevalence of overweight (defined as BMI $\geq$ 1SD in WHO child growth standards) or obese (defined as BMI $\geq$2 SD in WHO child growth standards) school-aged children is 20%, 5% of whom are obese (Branca et al., 2007). In the US, using the CDC definition of overweight (BMI $\geq 85^{th}$ percentile) and obesity (BMI $\geq 95^{th}$ percentile) these figures are 30% and 15%, respectively (Wang and Lobstein, 2006). Worldwide, it is estimated that 1 in 10 school-aged children (5 to 17 years old) are overweight or obese, using the WHO growth standards for definition (de Onis et al., 2012). There is a wide range of prevalence levels, with overweight (including obesity) prevalence in Africa, South East Asia and the South Pacific averaging below 10%, and in the Americas, Europe and the Eastern Mediterranean regions average above 20%. So the spread of obesity has been taking place at different speed across the world. In almost all developed countries (except Russia, and Poland), childhood obesity prevalence have been increasing more dramatically than other regions of the world. Moreover, countries that have been undergoing rapid economic transformation in the developing world show accelerated rate of childhood

obesity, particularly in urban societies, in higher socio-economic classes (Wang and Lim, 2012, Wang and Lobstein, 2006). These countries face the double burden of over-nutrition and under-nutrition (Wang and Lim, 2012). One scenario for the outcome of this double burden is having children with low birth weights and subsequent stunting, responding to future availability of food by increasing in weight disproportionately to height and increasing central adiposity and subsequently increasing the risk of related chronic diseases (Hassan et al., 2008, Wang and Lobstein, 2006).

The recent literature shows levelling off of the childhood obesity epidemic in some regions of the world (Rokholm et al., 2010). Recently, high quality evidence with descriptive datasets coming from Australia, China, England, France, the Netherlands, New Zealand, Sweden, Switzerland, and the USA with data from 467,294 children and adolescents aged 2-19 years where two measures of obesity were used to estimate the prevalence of paediatric obesity since 1999 suggests that the prevalence of overweight and obesity appears to be plateauing at different levels, however, sex, age, socioeconomic status and ethnicity determine the rate of change across those nations. Nonetheless, overweight and obesity remains at epidemic proportions (Olds et al., 2011).

In summary, the prevalence of paediatric obesity has been increasing worldwide with probable stabilisation more recently in western countries. The rate of spread differs between countries, and could be slowing in some parts of the world.

1.4 The aetiology of paediatric obesity

Although the mechanism of obesity development is not fully understood, it remains an energy balance disorder that is caused by an excessive energy intake over energy requirement; this is a simplified version of a more complex subject (Reilly et al., 2007). Measuring energy intake or examining energy expenditure in paediatrics is limited due to inaccuracy of the measurements used or their high cost, respectively (Reilly, 2006).

There are multiple factors for excess positive energy balance imbalance including genetics, environmental, lifestyle preferences and cultural factors (Kosti and Panagiotakos, 2006). So in other words, in order to identify aetiological factors of paediatric obesity, one could search for possible genetic and epidemiological risk factors (Reilly, 2006). From a review of systematic reviews of early-life determinants of overweight and obesity, figure 1.1

shows a model proposed by Monasta et al (Monasta et al., 2010) which displays the possible risk factors predisposing to paediatric overweight and obesity.

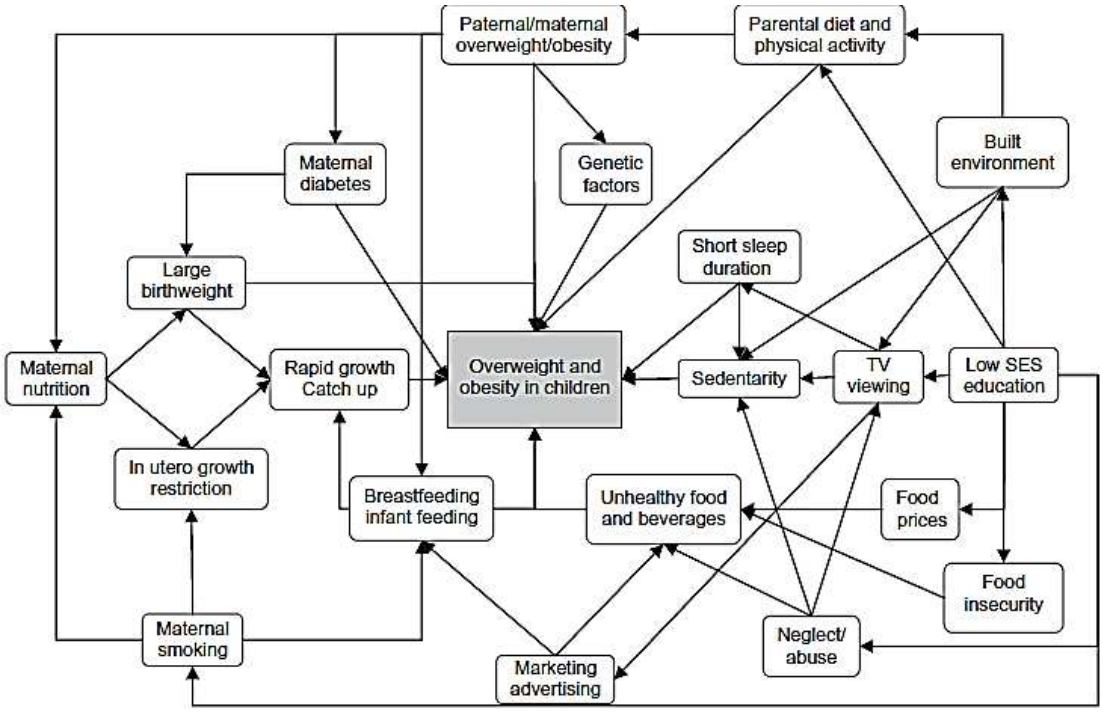

Figure 1. 1 The complex web of potential determinants of overweight and obesity in children. Source Monasta et al., 2010.

As discussed before, the great increase in paediatric obesity in the world over the past several decades suggest that environmental factors have greater influence on the aetiology than the genetic factors. The 'obesogenic environment' is a term used in the media and the literature to describe the current environment predisposing to chronic positive energy imbalance with readily available energy dense foods low in nutrients and discouraging physical activity(Swinburn et al., 1999). However, twin studies had shown that fat distribution of twins, monozygotic or dizygotic, were similar regardless of the environment in which they grew (Phan-Hug et al., 2012, Ramachandrappa and Farooqi, 2011, Stunkard et al., 1990) and so some genetic contribution exists.

1.4.1 Genetic contributions to obesity

Genetic contribution to obesity could be divided into single gene mutations in which obesity is the resultant abnormality, or genetic syndrome in which obesity is part of the identifiable signs of the specific medical syndrome along with mental retardation and developmental abnormality, or the result of multiple relatively common variants, each of which has small effect (Ramachandrappa and Farooqi, 2011).

Eating behaviour can be viewed as homeostatic mechanism that is controlled by hormonal signals from adipose tissue and the gastrointestinal tract to provide feedback to the hypothalamus to regulate appetite (Han et al., 2010). Gene mutations in the production, signalling or receptors of these hormones could contribute to the aetiology of obesity (Farooqi et al., 2007). Congenital leptin and leptin receptor deficiencies, and proopiomelanocrtin (POMC) deficiency are examples and share the phenotype of early onset severe obesity. The prevalence of these mutations has varied from 0.5% of obese adults to 6% in patients with severe childhood obesity (Farooqi et al., 2007).

It has been suggested that 20 to 90% of the variation in BMI is inheritable (Maes et al., 1997). However, studying the genetic basis of obesity susceptibility is difficult due to its complexity and polygenic nature. Single gene mutations are rare occurrences, with prevalence ranging from 0.5 to 4% of the population (Miraglia Del Giudice et al., 2002, Vaisse et al., 2000)

There are about 30 medical syndromes in which paediatric obesity is one of their signs (Holgate et al., 2012). Other signs and symptoms include dysmorphic features, mental retardation, short stature, and developmental abnormalities. These inheritable disorders explain about 1 to 2% of paediatric obesity (Lobstein et al., 2004). Down syndrome, Prader-Willi syndrome, Duchenne muscular dystrophy, Albright hereditary osteodystrophy, and Fragile X syndrome are some of these conditions that can be seen in clinical settings.

Single nucleotide polymorphism (SNP) is a variation in a single locus of DNA sequence in an individual which can result in impaired DNA coding resulting in a disorder or disease (den Hoed et al., 2009). The rs9939609 SNP in fat mass and obesity associated gene (FTO) is one example, contributing to 16% of obesity risk in the population (Frayling et al., 2007).

1.4.2 Endocrine disorders

The endocrine system is made up of glands in the body that produce hormones, which can act locally or at distant organs, in order to control body function, growth, sexual development and metabolism. There are several endocrine abnormalities that are associated with obesity (Nussey and Whitehead, 2001). Some of these abnormalities result in obesity as one of their signs; others are caused by obesity and can be corrected with

weight loss. Classically, these conditions include; hypothyroidism, growth hormone deficiency or resistance, hypopituitarism, hypogonadotrophic hypogonadism, hypogonadism, cortisol excess, pseudohypoparathyroidism, and craniopharyngioma (Nussey and Whitehead, 2001). In most of these cases, appropriate management of the primary cause can result in weight loss.

1.4.3 Birth weight, parental factors and foetal growth

Most obese adults were obese adolescents and most obese adolescents were overweight or obese children (Rooney et al., 2011). In a birth cohort of 777 infants, followed up for 20 years, Rooney et al. (2011) concluded that the relative risks (RRs) to predict obesity at early adulthood were 12.3 (95% CI 5.81, 26.1) for childhood and 45.1 (95% CI 17.24, 117.94) at adolescence. In fact, obesity can often be traced back to early childhood development (Maes et al., 1997). Children who develop adiposity rebound before the age of 5 years have increases in mean BMI from age 3 to adolescence, but those who experience later adiposity rebound have decreases in BMI from age 3 to adolescence. This pattern is maintained into adulthood (Williams and Goulding, 2009, Rolland-Cachera et al., 2006). More evidence from Bjerregaard and colleagues (Bjerregaard et al., 2014) from the Copenhagen Perinatal Cohort where participants were followed from birth to the age of 42 (n= 1633) showed that higher weight gain during the first 12 months of life was associated with higher adult BMI.

High birth weight is associated with increased fat and lean mass in infancy and childhood (Monasta et al., 2010). Small-for-gestational-age babies who show early catch-up growth might be at risk of childhood obesity and insulin resistance (Monasta et al., 2010).

Gestational diabetes produces macrosomia (large babies), and could be associated with childhood obesity later in life. A similar association is also found between prenatal maternal smoking and later childhood obesity (Monasta et al., 2010).

There are certain environmental settings that could predispose children to obesity. Growing up with an obese parent is a risk factor for subsequent obesity, especially if both parents were obese (Lobstein et al., 2004). There could be genetic as well as shared environmental factors in this picture. This relationship maybe stronger if the mother is obese (Nader et al., 2006).

Evidence from systematic reviews suggests that breastfeeding is likely to be causally protective against childhood obesity (Yang and Huffman, 2013).

1.4.4 Diet

Energy intake is one input of the energy balance equation, thus high energy intake is considered a risk factor for obesity development. Food preferences and eating habits that lead to obesity are gained during childhood from infancy onwards (Pearce and Langley-Evans, 2013). A recent review by Pearce and Langley-Evans (2013) on the relationship between foods consumed during infancy complementary feeding and overweight or obesity during childhood, found that only one study out of five showed that high energy intake in early infancy could be associated with high BMI and percentage body fat, so considered the results as inconclusive and further research is needed to establish the nature of the relationship between food consumed and eating habits acquired during infancy and obesity during childhood.

The source of the high energy intake is often from high fat content of food (Lobstein et al., 2004). Evidence from the past 50 years show that fat content of the modern diet has increased markedly, coupled with higher consumption rate and larger portion size especially for foods eaten outside the home (French et al., 2001). This pattern obviously can provide larger sum of energy to the child's actual need. In children who ate meals with high fat content from fast food consumed poorer quality diet than those who did not, and could increase their risk of obesity if this was allowed to be part of their lifestyle (Bowman et al., 2004). However, carbohydrate content of children diet has received little attention with the exception of sweetened soft drinks that show a positive association with the development of obesity in childhood (Lobstein et al., 2004, BMJ, 2012). This was also supported by a recent systematic review (Monasta et al., 2010).

1.4.5 Sleep deprivation

Monasta et al. (2010) in their review of systematic reviews on the association between sleep duration during infancy and the risk of future childhood obesity concluded that the shorter the period of sleep during infancy (< 12 hours of sleep) the more likely to encounter obesity later on in life (at the age of 7 to 10 years of age). This association was stronger for boys and for younger age children (<10 years of age).

1.4.6 Physical activity and sedentary behaviour

Systematic reviews have concluded that prolonged screen time and decreased level of physical activity was associated with increased body fatness (Monasta et al., 2010). Sedentary behaviour could also result from obesity as play and other physical activities are less attractive to the obese child (Tsang et al., 2013, Bauman et al., 2012). However, a longitudinal study of 871 children from the Auckland Birthweight Collaborative Study in New Zealand with a 7 year follow up confirmed that sedentary behaviour predicts overweight and obesity in children (Blair et al., 2007). This may work by displacing the amount of time a child would normally spend on play with inactivity and in doing so, the likelihood of consuming sugary drinks and energy dense foods could increase (Lobstein et al., 2004).

In summary, there are multiple risk factors that could predispose to the development of paediatric obesity. Some factors are at least potentially modifiable and others are not. In clinical settings, proper assessment of the obese child or adolescent and their family is essential in order to pinpoint the factor or factors that might have led to the development of obesity and offer the best possible treatment options and support (SIGN, 2010).

1.5 Complications of paediatric obesity

With the relatively recent and fast increase in paediatric obesity prevalence emerged multiple and dire health consequences both physical and psychological. These consequences could represent the roots of multiple diseases and disorders that can emerge in early adulthood, or can present in their full-blown picture in childhood and adolescence (Juonala et al., 2011, Reilly and Kelly, 2011, Lobstein et al., 2004). There are immediate health consequences of paediatric obesity and there are long-term health risks. All of these complications can be divided into either physical complications which can affect every organ system in the body, or psychological complications. The evidence for these associations from the literature is multiple and extensive.

Identifying children and adolescents with obesity in turn identifies a group of the population who suffer from cardiovascular disease risk factors, and inflammatory and metabolic risk factors, and who might also suffer from multiple psychosocial impairments (Reilly et al., 2003). However, as discussed in section **1.1 Definition of paediatric obesity** above, an ideal definition of paediatric obesity is still not available due to a number of reasons; lack of agreement on a universal anthropometric tool to classify healthy weight,

overweight and obesity ranges, lack of agreement on a reference population being national or international, and lack of agreement on the most appropriate cut off points that best mark the individuals who are at a higher risk of obesity-related complications (de Onis and Lobstein, 2010).

Figure 1.2 outlines the physical and psychological complications of childhood obesity. Out of the vast number of complications, the psychological complications are probably the most common (Reilly, 2006). These include depression, anxiety disorders, low self-esteem and low health related quality of life (HRQL).

One important consideration made by Ebbeling and colleagues (2002) is that the occurrence of these obesity-related complications can be affected by ethnicity as a result of cultural factors, one example being that psychological consequences are higher in whites than other ethnic groups in a study done with regards to self-esteem in girls in the USA (Kimm et al., 1997). Ethnic minorities and socioeconomic disparities have been linked to childhood and adolescent obesity in several parts of the world (Singh et al., 2008b, Stamatakis et al., 2005, Willms et al., 2003). However, in Kuwait there is no official socioeconomic categorisation of the population (Shah et al., 1998) and questions pertaining inequalities in the society have not been answered in a systematic manner. Moreover, published census data from the Public Authority for Civil Information (PACI) has no reference to ethnic categorisation for the population, related to the fact that the Kuwaiti population is homogenous of Arabic origins.

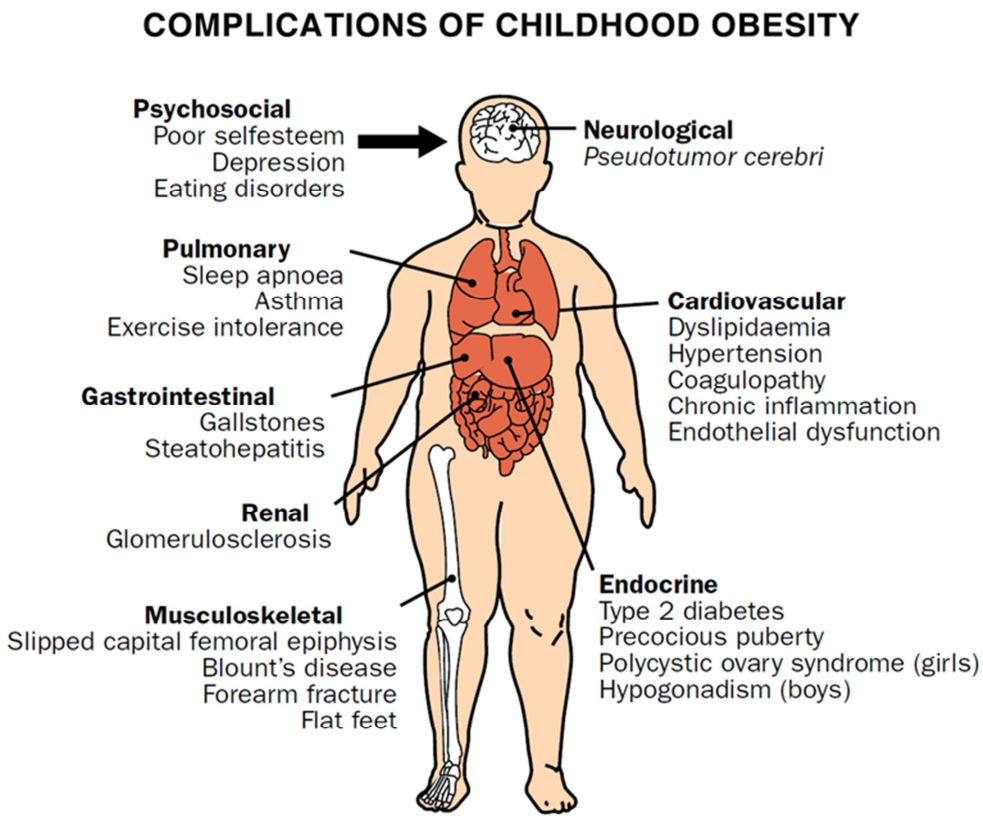

Figure 1. 2 Complications of childhood obesity. Source Ebbeling et al., 2002.

1.5.1 Psychological complications

Some researchers argue that obesity should be regarded as mental or behavioural disorder, and that research should be directed towards identifying the psychological factors associated with its development rather than identifying medical strategies for prevention and treatment (Russell-Mayhew et al., 2012). However, not all obese children and adolescents suffer from psychosocial problems, and the lack of longitudinal studies in this area hinders the recognition of the direction of the relationship between obesity and psychosocial issues and also the magnitude of such relationship (Vila et al., 2004).

In a cross-sectional study done by Vila and colleagues (2004) on 155 obese children and adolescents attending obesity treatment in Paris (aged 5 to 17 years) to explore the relationship between paediatric obesity and psychopathological disorders, the researchers showed that obesity is a significant factor in the development of psychological disorders namely separation anxiety and social phobia and incompetence, which all may contribute to the maintenance of obesity. When this sample was compared with diabetic controls (Type 1 diabetes which a major part of their management relies on dietetic control), they had significantly more psychological disorders in number and severity. In another study that supports the view that obesity could involve greater potential for psychosocial distress

than some chronic somatic disorders, Schwimmer et al. (2003) recruited 106 children and adolescents aged 5 to 18 years, and studied HRQL of this sample using the PedsQL™ questionnaire, which is a valid and reliable age specific health related quality of life questionnaire (Varni et al., 2001), and compared it with the results from cancer paediatric patients. The researchers found that HRQL levels were worse for the obese group. For obese children and adolescents, psychosocial development is usually impaired to a varying extent ranging from dissatisfaction with weight status and shape to low self-esteem, depression and other psychosocial disorders (Griffiths et al., 2010) (discussed in more details in chapter 4).

1.5.2 Cardiometabolic complications

The major cardiovascular disease risk factors that can be found in children and adolescents are hypertension, dyslipidaemia, left ventricular hypertrophy or dysfunction, hyperinsulinaemia and /or insulin resistance (Reilly et al., 2003). The Bogalusa Heart Study in Louisiana (Freedman et al., 2007) had provided detailed profile of cardiovascular risk factors in children and adolescents and their persistence into adulthood. In the study, obese adolescents (BMI ≥ 99th percentile, Centre for Disease Control (CDC) growth charts) had the prevalence of hypertension increased 8.5 fold, the prevalence of total serum cholesterol increased by 2.4 fold, and a 3 fold increase in LDL cholesterol, as adults aged 27-31 years.

The metabolic syndrome (insulin resistance syndrome or syndrome X) is a combination of medical disorders that, when present, increase the risk of cardiovascular disease, stroke and diabetes. There have been debate on the proper definition of metabolic syndrome in adults and whether all the features of the syndrome should be obligatory for the definition, however, in 2009 the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity reached a Joint Interim Statement to harmonise the definition of the syndrome. There are 5 criteria in use, and if 3 out of these 5 are present, that would qualify for the definition (Alberti et al., 2009). These criteria include; elevation of waist circumference (population-specific definitions), triglycerides ≥ 1.7 mmol/L or drug treatment for elevated triglycerides, reduced HDL < 1.0 mmol/L in males or < 1.3 mmol/L in females or drug treatment for reduced HDL, elevated systolic blood pressure ≥130 mmHg and/or diastolic blood pressure ≥ 85 mmHg or treatment for hypertension and

elevated fasting blood glucose ≥ 5.6 mmol/L or drug treatment for diabetes mellitus (Alberti et al., 2009).

The diagnostic criteria for childhood and adolescent metabolic syndrome are not unanimously agreed upon (Goodman et al., 2007) due to the fact that the paediatric risk profile is unstable in the short (60 days) and long (1.5 year) term based on the adult criteria (Gustafson et al., 2009). Applying absolute cut off points to continuous variables without considering the impact of aging, pubertal stages, and ethnicity are also factors in failure to reach a consensus. Nevertheless, identifying children and adolescents with increased risk of developing cardiovascular disease later on is extremely important and one of the available clinical definitions for paediatric metabolic syndrome is the IDF definition of metabolic syndrome in children and adolescents which consist of five criteria (Zimmet et al., 2007). These guidelines are age-specific to encompass the different stages of paediatric development. They start from 6 years of age to older than 16 years of age as shown in box 1.1. However, the IDF recommend that the syndrome should not be diagnosed at age 10 and younger, and such patients with identified criteria should be directed towards obesity treatment instead as appropriate. To be diagnosed with MS using the IDF definition, high waist circumference (population specific percentile) and two other criteria need to be present.

Al Isa and colleagues assessed the prevalence of metabolic syndrome in a random sample (n=431) of female Kuwaiti adolescents aged 10 to 14 years using IDF criteria (Al-Isa et al., 2010a). The results showed a high prevalence of metabolic syndrome in that age group (14.8%) compared to general population.
Internationally, a recent review by Tailor et al (2010) concluded that prevalence of MS among in the paediatric population ranges from 1.2 and 22.6%, where obesity is the most important risk factor (up to 60% of the obese children or adolescents maybe affected according to Tailor et al., 2010).

Box 1.1 IDF definition of at risk group and of metabolic syndrome (MS) in children and adolescents

Age 6 to < 10 years

· Obesity ≥ 90th centile defined by waist circumference

· MS should not be diagnosed, further measurements should be made if family history of MS, type 2 DM, dyslipidaemia, cardiovascular disease, hypertension or obesity.

Age 10 to < 16 years

· Obesity ≥ 90th centile or adult cut off if lower assessed by waist circumference

· Triglycerides ≥ 1.7 mmol/L

· HDL-C < 1.3 mmol/L

· Blood pressure ≥ 130mmHg systolic or ≥ 85mmHg diastolic

· Glucose ≥ 5.6 mmol/L (oral glucose tolerance test) or known type 2 diabetic

Age > 16 years

· Use existing criteria for adults

Source Zimmet et al. 2007.

1.5.3 Orthopaedic complications

Excess weight is a continuous stress on the musculoskeletal system. The presence of unfused growth plates and softer cartilaginous bones of children contribute to the development of a number of abnormalities including; slipped femoral capital epiphyses, Blount's disease (Bowing of legs and tibial torsion) and osteoarthritis in older children and adolescents (Wills, 2004). Moreover, extreme paediatric obesity is associated with increased chances of lower extremities fractures (Kessler et al., 2013).

1.5.4 Endocrine complications

Childhood and adolescent obesity is associated with increased incidence of insulin resistance and type 2 diabetes mellitus. In some populations, type 2 diabetes mellitus in adolescents account for 50% of the newly diagnosed cases (Fagot-Campagna, 2000).

Moreover, the pre-diabetic state i.e. glucose intolerance and insulin resistance, seems to be more prevalent in the severely obese children and adolescents, irrespective of ethnic origin (Sinha et al., 2002). In view of the subsequent increase in blood glucose, emerges the possibility of the macro-vascular and micro-vascular impairments of type 2 diabetes mellitus that include complications like stroke and kidney failure, respectively.

Menstrual abnormalities are often diagnosed in obese female children and adolescents, one of which is the decreasing age of menarche (before 11 years of age) (Currie et al., 2012, Must and Strauss, 1999). In Kuwait, Al Awadhi et al. (Al-Awadhi et al., 2013), had investigated the age at menarche for 1250 contemporary girls and found a significant inverse relationship between the age at menarche and obesity or overweight before and after adjusting for potential confounders. In males however, the evidence is not clear whether obesity reduces or increases the age of puberty (De Leonibus et al., 2012).

Oligo- or amenorrhoea, hirsuitism, obesity, acne, acanthosis nigricans, and insulin resistance are all part of the polycystic ovarian syndrome (PCOS) formally known as Stein-Leventhal syndrome (Ojaniemi et al., 2010). Pre- and peripubertal obesity could be a contributing factor in the development of PCOS in adolescents through insulin-resistant hyperinsulinism (Rosenfield, 2007). The mechanism of this process is yet unknown, however, studies showed that using insulin-lowering agents such as metformin administered to obese girls at risk of developing PCOS, improved insulin resistance, adiposity and androgen levels (Ibanez et al., 2004).

1.5.5 Respiratory complications

In a recent review by Pulgaron (2013) examining the relationship between obesity and other comorbidities, the prevalence of asthma has been increasing in parallel with obesity epidemic in recent years. Obesity seems to increase the incidence of asthma or worsen existing asthma. There are some suggestions of gender differences in the relationship between obesity and asthma but the evidence is not yet consistent.

Sleep-associated breathing disorders ranging from heavy snoring to obstructive sleep apnoea have also been associated with paediatric obesity. The resultant hypoxaemia of sleep-disordered breathing can predispose to increase in inflammatory risk factors (Tauman et al., 2007, Tauman and Gozal, 2006). It has been estimated that 94% of children with severe obesity have abnormal sleep pattern (Silvestri et al., 1993). The state of

hypoxia and hypercapnia that results from obstructive sleep apnoea can potentiate the development of cardiovascular abnormalities (Daniels et al., 2005).

1.5.6 Gastrointestinal complications

Gastroeosophogeal reflux disease (GERD) is a common complication of obesity in adults affecting almost 40% of the population (Anand and Katz, 2010). With the rising of paediatric obesity and extreme obesity, GERD has been diagnosed more frequently in obese children and adolescents (Koebnick et al., 2011). In addition, gallstone disease is found to be high in prevalence in extremely obese children and adolescents, especially girls (Koebnick et al., 2012). Non-alcoholic fatty liver disease (NAFLD) is the most prevalent chronic liver disease in obese children and adolescents (Giorgio et al., 2013). It is associated with the development of insulin resistance and type 2 diabetes mellitus, metabolic syndrome, hypertension and cardiovascular disease (Koebnick et al., 2009). Early recognition is needed to avoid future morbidity and mortality (chapter 5).

1.6 Paediatric obesity prevention

The ultimate goal of any health promotion strategies is to modify human behaviour that is causing ill health into more health-enhancing behaviour to reduce the risk of disease. However, behaviour modification goes beyond individual level to include more societal and broader community levels and any health promotion plan should be injected at these levels for potential change (Lawlor and Pearce, 2013). There is a wealth of trials on interventions to prevent childhood obesity in school settings, with successful outcomes (Martin et al., 2013, Katz et al., 2008, Sahota et al., 2001b). The rationale behind this is that schools are well circumscribed areas, where children spend substantial proportion of their lives and in most countries of the world education is compulsory (Nixon et al., 2012, Katz et al., 2008).

It is beyond the scope of this thesis to examine the prevention interventions as our main theme is paediatric obesity treatment. The most recent Cochrane review on the prevention of child and adolescent obesity was that of Waters et al (2011).

1.7 Paediatric obesity treatment

Management of paediatric obesity and its related health risks consume more and more time of health professionals, presenting a health care challenge (Avis et al., 2014, Story et al., 2002). However, the need for evidence-based interventions for obesity treatment is important in order to counteract the current paediatric obesity epidemic and its related

health consequences. The current knowledge, belief and practices of physicians at secondary health care in the western world lacks the proper training in lifestyle modification required to deal with behavioural problems which maintain paediatric obesity (Avis et al., 2014, Klein et al., 2010, O'Brien et al., 2004, Foster et al., 2003, Story et al., 2002).

1.7.1 Why treat paediatric obesity?

There are a number of high priority reasons to treat childhood and adolescent obesity some of which are as follows:

- Childhood and adolescent obesity does not spontaneously resolve. Strong evidence from various prospective studies show that childhood and adolescent obesity tracks into adulthood and the evidence is strongest with increasing age; over 50% of obese adolescents become obese adults (Singh et al., 2008a, Guo et al., 2000, Whitaker et al., 1997).
- Obese children and adolescents already experience multiple physical and psychological consequences as a result of their obesity as explained in section **1.5 Complications of paediatric obesity** above.
- Adverse cardiovascular risk factors encountered during childhood and adolescence increases the risk of adult cardiovascular disease morbidity and mortality (Reilly and Kelly, 2011, Reilly et al., 2003).
- Management of childhood and adolescent obesity can improve the cardiovascular risk factor profile. Decreasing one's weight by 6.5% leads to a decrease in health risks in adolescents as well as adults (Shapiro et al., 2006). Furthermore, the atherogenic profile and insulin sensitivity in obese children improves with a 0.5 reduction in BMI SDS over 1 year period (Reinehr and Andler, 2004, Reinehr et al., 2004).
- Improvement in psychosocial functioning can also be attained with proper weight management of childhood obesity (Hofsteenge et al., 2013, Harris-Glocker et al., 2010, Lofrano-Prado et al., 2009, Myers et al., 1998).
- With the current prevalence and severity of childhood and adolescent obesity, the economic cost has increased dramatically, and the costs are likely to increase even more (Wang and Dietz, 2002) and weight management programmes could be designed to be cost effective or even cost saving (John et al., 2012).

1.7.2 Current recommendations for paediatric obesity treatment

The current recommendation for paediatric obesity treatment derived from systematic reviews, notably from the most recent Cochran review (Oude Luttikhuis et al., 2009). The review included 64 studies; 54 lifestyle intervention studies and 10 on drug treatment. However, long-term outcomes (follow up period of ≥ 6 months following the intervention) of obesity treatment was limited, hence the recommendation in the Cochrane review to extend the trial period in order to examine the efficacy of the proposed interventions in the longer-term.

The expert committee on the treatment of overweight and obesity in children and adolescents in the USA recommends that the treatment of obesity should start at younger age (Spear et al., 2007). Age is an important predictor of weight management success in children and adolescents; younger children seem to achieve more weight loss (Danielsson et al., 2012, Pott et al., 2009, Goossens et al., 2009, Sabin et al., 2007).

1.7.3 Who should be offered treatment?

Ideally, all children and adolescents who suffer from obesity, as defined by local protocols, should have a weight management plan (Spear et al., 2007). Identification of obese children and adolescents should be made at primary care level, and special attention should be directed towards assessing the health risks associated with the condition as well as assessing unhealthy lifestyle habits that could have led to the child's or adolescent's obesity (Barlow, 2007). The focus should be on the family as a whole and not just the child or the adolescent. Suggestions for obesity management plan through lifestyle modification can be made at this primary setting.

1.7.4 Obesity treatment goals

The primary treatment goal is to improve the long-term physical health through permanent healthy lifestyle habits. In children and young adolescents who have growth potential and do not suffer from co-morbid conditions associated with their obesity, weight maintenance is the goal of the treatment plan which in turn allows for normal growth in height to take place and "cure" the child as he/she grows (SIGN, 2010).

In children and adolescents where faster weight reduction is needed due to the presence of obesity-related co-morbid conditions including psychosocial functioning, weight loss is the goal (SIGN, 2010). Therapeutic goals are also considered such as correcting metabolic abnormalities, improving psychosocial health and family functioning.

1.7.5 How strong is the evidence on the effectiveness of obesity treatment?

In general, poor dietary habits, decreased physical activity and sedentary lifestyles play a fundamental role in the onset of overweight and obesity (Lobstein et al., 2004). Therefore most behavioural interventions for obese children and adolescents are aimed at improving lifestyle behaviours and there is evidence of efficacy of lifestyle modification in the Cochrane review (Oude Luttikhuis et al., 2009). Accordingly, lifestyle modifications usually include three components: dietary intake, physical activity and sedentary behaviour reduction. Changing human behaviour is very challenging task especially in an environment that favours sedentary behaviour and fat and sugar loaded fast foods (Spruijt-Metz, 2011).

Four recent reviews on interventions to treat childhood and adolescent obesity (Ho et al., 2012, Oude Luttikhuis et al., 2009, McGovern et al., 2008, Atlantis et al., 2006) had reviewed very diverse studies comprehensively (Table 1.2). Ho et al (2012) performed a systematic review and meta-analysis on the effectiveness of lifestyle interventions (dietary and physical activity modifications) on weight change (BMI or BMI Z score) in children and adolescents ≤ 18 years of age. Other outcomes included lipid profile, serum insulin and blood pressure. A total of 33 studies included, mostly from the USA, and the rest were from Australia, Israel, Germany, the UK, Belgium, China, Finland, Iran, Korea, Mexico, Taiwan and Tunisia. Ho and colleagues concluded that lifestyle interventions had direct effect on weight loss, improvement in the lipid profile, fasting insulin and blood pressure as compared to no treatment control. However, more research is needed to determine the optimal duration, frequency and long term benefits of lifestyle intervention in the treatment of paediatric obesity (Ho et al., 2012).

The 2009 Cochrane review of interventions to treat obesity in children and adolescents showed that family-based programmes achieve the best results in relation to weight reduction, as mentioned above (Oude Luttikhuis et al., 2009).

McGovern et al. (2008) reviewed 61 trials that were designed for treating childhood and adolescent obesity non-surgically including pharmacological trials, dietary interventions, physical activity interventions and combination of dietary and physical activity modifications. The efficacies of these interventions were short-term with no or limited subsequent follow up; however, non-significant trends favoured combined lifestyle interventions with parental involvement.

Atlantis and colleagues (2006) studied the effects of 14 exercise trials in the treatment of childhood and adolescent obesity. They recommended between 155 to 180 mins/week of

moderate to vigorous aerobic exercise to reduce adiposity in obese children and adolescents.

All four reviews call for future larger scale trials with long-term follow up and broader health and psychosocial benefits.

However, data on the effectiveness of comprehensive weight management programmes for the treatment of adolescent obesity are limited (Danielsson et al., 2012), Community and school programmes often have dual goals of prevention and treatment, so the data are difficult to evaluate (Zitsman et al., 2014, Brei and Mudd, 2013).

Tabel 1.2 Reviews of obesity treatment trials

Source	Number of studies	Inclusion criteria	Studies that significantly reduced adiposity or BMI	weight maintenance
Ho et al 2012	33 trials in the meta-analysis outcomes included BMI, BMI Z score, lipids profile, fasting insulin, blood pressure	RCT on lifestyle interventions overweight or obese age ≤ 18 years lifestyle interventions vs: usual care, waiting list, no treatment or written material	Significant weight loss Significant improvement in lipids profile, fasting insulin, and blood pressure	Significant post treatment effect after 1 year significant improvement in lipid profile, fasting insulin and blood pressure after 1 year
Oude Luttikhuis et al. 2009	64 trials in the review 54 on lifestyle interventions 10 on drug therapy 8 lifestyle and 4 drug trials used for meta-analysis	RCTs of lifestyle, drug and surgical interventions +/- family members involvement Age under 18 years min 6 months follow up (3 for drug therapy) Exclude; eating disorders, type 2 diabetes, secondary causes of obesity	5 out of 8 lifestyle trials 3 out of 4 drug trials	Long-term effects of obesity treatment was limited recommend more high quality studies
McGovern et al. 2008	76 trials in the review 61 trials in the meta-analysis: 9 on drug therapy 6 on Dietary interventions 17 on physical activity 23 on combined lifestyle interventions	RCTs Drug or lifestyle interventions Exclude; type 1 diabetes, eating disorders, obesity syndromes	6 out of 9 drug therapy 4 out of 6 Dietary interventions 5 out of 17 physical activity interventions 6 out of 23 combined lifestyle interventions	There was limited evidence that medications and lifestyle interventions reduced paediatric obesity in the short term. The long-term effectiveness effectiveness and safety was unclear
Atlantis et al. 2006	14 Physical activity interventions	RCTs, age under 18 years Could include nutrition intervention report pre and post treatment change in overweight	2 out of 14 studies	Future research is needed to evaluate dose-response effect, long-term and multiple health outcomes

BMI: body mass index; RCTs: randomised controlled trials; Lifestyle interventions: dietary, physical activity and behavioural interventions

Drug therapy: orlistat, Sibutramine, Metformin

The expert committee on the treatment of overweight and obesity in children and adolescents from the USA (Barlow, 2007) suggests one possible scenario with four-staged approach, depending on the severity of the condition and the willingness of the family to commit. The first stage called prevention-plus where the health professional, at primary care level, analyse the eating and lifestyle habit and offer healthy eating habit and to increase the level of physical activity of the individual while reducing sedentary behaviour. The second stage could be started first if obesity was severe or was associated with co-morbid conditions. It is a structured weight management plan that could involve more than one heath professional usually a dietician and physical therapist, with hospital OPD referral to a qualified physician.

The third stage is a comprehensive multidisciplinary intervention approach with more frequent hospital OPD visits and intensive monitoring for behavioural change and setbacks. The multidisciplinary team include a qualified physician, a dietician, a physical therapist, and a psychologist. Hospital appointments are frequent to ensure better compliance and health improvement.

The last stage is a tertiary care intervention and should not be started unless the patient had failed in the third stage and it only concerns those with morbid obesity and associated co-morbid conditions because it involves the use of medications and/or surgery and/or hospital admission.

1.7.6 Dietary component

There is no straight forward guideline as to what dietary regimen works best in children and adolescents to treat obesity (Spruijt-Metz, 2011). The aim is to replace energy-dense foods of low nutritious value with low-energy foods with high nutritious value (Steinbeck, 2005). The dietary interventions that have been reported in recent reviews include low-glycaemic index diets, protein-sparing modified diets, low-carbohydrate diet, high-protein diet and hypocaloric diets (McGovern et al., 2008).

The Epstein group from the USA reports the majority of studies and are the most frequently cited in the literature (Epstein et al., 2012, Epstein et al., 2001, Epstein, 1996, Epstein et al., 1995a, Epstein et al., 1985). Their interventions are resource intensive and characterised by long-term follow-up, include a traffic light diet scheme, increase in physical activity and decrease in sedentary behaviour, and usually involve a family member (Epstein, 1996). Stewart and colleagues (2005) simplified the traffic light scheme developed by Epstein et al (1985) and this was used in the Scottish Childhood Obesity Treatment Trial (SCOTT) in 2008 (Hughes et al., 2008, Stewart et al., 2005, Epstein et al.,

1985). This modified version of the traffic light diet used basic divisions of foods into 3 categories without residing to the concept of calorie counting, therefore, the concept seemed simpler and easier to follow by parents and their children. Figure 1.4 displays the food categories of the modified traffic light diet where "red" refers to bad foods namely energy-dense high fat high sugar foods, "green" refers to good foods namely fruits and vegetables and "amber" is for foods restricted to meal times.

Red foods[a]	Amber foods[b]	Green foods[c]
• Fried foods • Potato chips • Pies, pastries • Take-out meals • Fries and burgers • Sugar • Sweets • Chocolate • Chocolate biscuits • Fancy biscuits • Cakes • Sugar-sweetened drinks • Desserts • Sugar- or honey-coated breakfast cereals	• Lamb, pork, beef • Sausages and burgers • Chicken and turkey • Fish • Eggs and cheese • Vegetarian meals • Bread/chapatti • Potatoes • Rice • Pasta • Plain breakfast cereals Low-fat alternatives of • Milk • Butter/margarine • Yogurts	• Fresh/dried fruit • Tinned fruit in fruit juice • Vegetables/salad • Homemade/tinned vegetable soup • Sugar-free gelatin • Plain breakfast cereals and low-fat milk • Plain popcorn, breadsticks • Sugar-free lollies • Diet or sugar-free drinks

[a]Long-term aim to be restricted to one per day.
[b]Recommended to be restricted to meal times.
[c]To be taken freely and substituted for red foods.

Figure 1. 3 Summary of the traffic light diet. Source Stewart et al., 2005.

1.7.7 Physical activity and sedentary behaviour

Increasing physical activity deals with the "energy out" part of the energy equations for weight balance. Hence, lifestyle interventions that incorporate increase in physical activity level as well as healthier dietary modifications reach far better results than interventions that focus on physical activity or diet alone (Oude Luttikhuis et al., 2009). On the other hand, although it may not have a dramatic impact on weight reduction, increasing physical activity alone will reduce obesity-related co-morbidities (O'Donovan et al., 2010, Ortega et al., 2008).

There is a general consensus that physical activity should be increased to 60 minutes per day of moderate to vigorous intensity activity and to decrease sedentary behaviour, often referred to as screen time, to less than 120 minutes per day (Health, 2011, O'Donovan et al., 2010, SIGN, 2010, Barlow, 2007, NICE, 2013).
Evidence also suggests that decreasing sedentary time is associated with decreased physical and psychological health risks and could lead to reduction in weight (Tremblay et al., 2011, Salmon et al., 2011).

1.7.8 Behavioural modification

The treatment of obesity requires lifestyle change, and this is done through change in behaviour, i.e. replacing obesity-enhancing sedentary and unhealthy dietary behaviours with health promoting behaviour. Robinson's review on behavioural treatment of childhood and adolescent obesity (Robinson, 1999) describes several components of behaviour change approach for the treatment that includes:

- Self-monitoring.
  This includes monitoring body weight, behaviour related to eating and physical activity, which in turn enhances self-awareness and control (Stewart et al., 2009, Robinson, 1999).

- Goal setting and contractual agreement, with rewards for reaching goals.
  Choosing an appropriate goal is determined by the child or adolescent in parallel with his or her ability to commit. The goal should be small, measurable, attainable, recorded and timed (Robinson, 1999). In line with this plan, a contract should be signed between the caregiver and the child or adolescent regarding this chosen goal, and if it is achieved within the time frame that was agreed upon, then a reward should be presented to the "winner" and that should not involve food or money. The reward technique represents a positive reinforcement method for the achievement and maintenance of goals (Stewart et al., 2009, Robinson, 1999).

- Skills to deal with high risk situations and relapses.
  There are a number of situations where commitment to goals could prove to be very difficult and requires skills in order to prevent relapse. These include parties, holidays, eating out and others (Stewart et al., 2009, Robinson, 1999)

- Stimulus control
  This involves controlling stimuli that can bring about the unhealthy behaviour. Establishing new routines that promote healthy eating and physical activity should replace old routines that promote unhealthy eating and sedentary behaviour (Stewart et al., 2009, Robinson, 1999).

Parental involvement with positive impact on the behavioural change approach is an important management aspect in all international guidelines (SIGN, 2010, Barlow, 2007, NICE, 2013). In fact, targeting parents as the agents of change in a weight management programme by Golan et al (1998) had a greater positive effect on the weight change of their primary school aged children than did the control who received group intervention. In this age group particularly, having a parent-only approach overcome the possibility of causing anxiety and stigmatisation to the child as a result of their weight management plan (Golan et al., 1998b).

1.7.9 More intensive treatment options

Morbidly obese adults are usually offered more intensive treatment options which would include pharmacotherapy, surgery or very low-energy diets (VLEDs). Some of these treatments have been recommended recently for morbidly obese adolescents (SIGN, 2010, NICE, 2013).

1.7.9.1 Pharmacotherapy

It is always recommended to start drug therapy in conjunction with dietary, lifestyle and behavioural modification (SIGN, 2010, NICE, 2013).

Orlistat (Genentech USA) is a reversible gastric and pancreatic lipase inhibitor that limits the gastrointestinal absorption of dietary cholesterols by about 30% (FDA, 2010b). It also causes a reduction in plasma fat-soluble vitamins hence concomitant administration of multivitamin supplement is recommended (FDA, 2010b). Orlistat should be part of low fat diet in order to have the desired caloric deficit to cause weight reduction. A number of studies have shown that orlistat can be effective in the treatment of adolescent obesity with significant decrease of BMI from baseline ranging from 0.5 to 4.1 kg/m² (Matson and Fallon, 2012). It is currently approved in USA for use in children > 12 years of age.

Sibutramine was formerly considered as a potential agent for weight management in morbidly obese adolescents through its satiety and thermogenic effects (Reisler et al., 2006, Godoy-Matos et al., 2005). However, in 2008 the FDA recommended that Abbott Laboratories withdraw Sibutramine from the market in light of the increased risk of adverse cardiovascular events that accompanied the sirbutamine Cardiovascular Outcome (SCOUT) trial (James et al., 2010, FDA, 2010a).

Metformin is an oral hypoglycaemic agent. Its use for weight management in children and adolescent has limited evidence from the literature (Matson and Fallon, 2012). However, it would be the first drug of choice for obese adolescents with type 2 diabetes, or the risk of type 2 diabetes , or with polycystic ovarian syndrome or even to reduce the weight gaining effect of psychotropic medication (Matson and Fallon, 2012). For adolescents, the use of metformin as adjuvant therapy with lifestyle modification has been recommended for its associated improvement in weight status and insulin sensitivity (Kendall et al., 2014).

1.7.9.2 Surgery

The NICE (2006) obesity management guidelines recommended bariatric surgery in children and adolescents only in exceptional circumstances with full psychological pre-operative evaluation and only if the candidate was close to physiological maturity (NICE, 2013). Moreover, the International Pediatric Endosurgery Group has published guidelines for pre-, intra- and post-operative surgical management of adolescent obesity (IPEG, 2003). They recommend preoperative education on the post-operative nutritional and exercise programmes that the patient should follow to maximize long-term success, as well as a life-long medical supervision with a team that includes the surgeon, a dietician, a psychologist and exercise therapist. A number of case series have been reported on bariatric surgery for adolescent obesity utilizing gastric bypass, vertical-banded gastroplasty and laparoscopic banding (Inge et al., 2004). A recent review and meta-analysis by Black and colleagues (2013) selected studies done on children and adolescents from 1955 to 2013 and showed that the 23 studies included in the meta-analysis had inconclusive reports on post-operative complications, however, BMI reduction after 1 year post surgery was significant (Black et al., 2013). Improvement in metabolic and psychological outcomes was also significant. As the current NICE guidelines provide general suggestions for the medical care plan, Black and colleagues urges the need for more specific, patient tailored plan with the appropriate choice of the surgical method according to physiological and psychological maturity of the patient.

1.7.9.3 Very Low Energy Diets (VLEDs)

Being liquid meal replacement or a protein-sparing modified fast (PSMF), VLEDs have been used in the treatment of adolescent obesity (Stallings et al., 1988, Brown et al., 1983). In PSMF, protein is the major component with 1.5 and 2.5 g/kg BW/day with the addition of vitamins and minerals, vegetables and water. Minimal carbohydrates may be added to avoid the possible negative nitrogen balance. The National Health and Medical Research Council for Australia (2003) advised that VLEDs be restricted to use in adolescents with significant morbid obesity (NHMRC, 2003).

1.7.10 Group versus individual treatment for childhood and adolescent obesity

One can argue that group therapy can be more efficient and less expensive to administer, as well as fostering more beneficial interactions between group members. Unfortunately, there is not much data directly comparing the results of group versus individual therapy. One RCT by Kalavainen et al. (2007) examined the effect of group based treatment for childhood obesity compared to the effects observed from receiving routine individual counseling. They recruited seventy 7 to 9 year old children, 35 of which received the routine treatment and the other 35 received the group treatment. The group treatment was composed of 15 sessions held separately for parents and children. Each session was given a special theme and carried health promotion messages related to diet, physical activity and behaviour modification techniques. One limitation to this study was the duration of the intervention, as the sessions extended for a period of 3 months and follow up only occurred after 6 months from baseline. The drop-out rate was low (n=2). The most important finding was that there was a significant drop in weight for height, BMI and BMI Z score in the intervention group compared to the control group (Kalavainen et al., 2007). Joined with this optimism is another high quality RCT by Savoye and colleagues (2007) which examined the effects of a group-based weight management programme (Bright Bodies) on weight, BMI and insulin resistance. The results for the intervention group were superior to the control group who received traditional weight management counselling. Their intervention was based on group therapy delivering exercise, nutrition and behaviour modification techniques. At 12 months follow up, these results persisted although drop-out rate was high (29%). There is still however an unanswered question in group therapy sessions which is related to an important and marked psychosocial morbidity associated with childhood and adolescence obesity which is whether group therapy programmes alleviate some of these morbidities by improving and developing the social skills among individuals in the group (Savoye et al., 2007).

In summary, treatment of paediatric obesity is important. The management plan involves lifestyle modification with dietary and physical activity interventions and should involve behavioural modification techniques. It probably requires some participation of the entire family. More intensive measures could be required in the case of severe obesity with co-morbid conditions. More research is still needed to establish a general protocol for the management of paediatric obesity and more training is required to update health professionals on the latest advances and guidelines for the treatment of paediatric obesity.

1.8 Kuwait in context

Kuwait is a small Middle Eastern country located at the North Western tip of the Arabian Gulf. It shares borders with Iraq on the North and West, Saudi Arabia on the South and West and the Arabian Gulf on the East. Its land of 17,818 km² consists mainly of parched desert, and over 90% of the country's population lives within the 500 km² area surrounding Kuwait City and its harbour (MOI, 2009).

The climate is extremely hot during the summer which extends from April to September, with temperatures exceeding 50°C during the day. The months of August and September experience moderate humidity. The highest temperature in January, the coldest month in the year, is typically 13.5°C. Annual rainfall is usually less than 160 mm per year, mostly falling in the winter season (FAO, 2008).

Administratively, Kuwait is divided into six governorates; Al Ahmadi, Al Farwania, Capital, Al Jahra, Hawalli and Mubarak Al Kabeer.

Kuwait's economy is dominated by the oil industry and its revenues. It has limited fresh water resources, thus desalination facilities provide most of the water for human consumption. Agriculture is limited by the lack of water and arable land. Aquatic resources, fish and crustaceans are plentiful in the Gulf.

1.8.1 Population:

On 31st December 2008 the population of Kuwait was 3,441,813, of which 32% were Kuwaiti nationals. Among the non-Kuwaiti population, 28% are Arabs, 65% are non-Arabs (mainly Asians) and 7% are stateless. The ratio of males to females among the total population was 1.5: 1 due to the large proportion of single men among the immigrant work force in the country (Table 1.3) (PACI, 2008).

The Kuwaiti population is a young population with approximately 40% below 20 years of age. The crude birth rate of Kuwaitis is high. Of note, Kuwait is an urban country with almost 90% of the population living in urban areas (MOP, 2007).

1.8.2 Economy

Kuwait is a small, rich, relatively open economy with 10% of the world reserves of crude oil. Petroleum accounts for nearly half of Gross domestic product (GDP), approximately 95% of export revenue and 80% of the government income. In 2005, GDP was 53.31 billion, giving Kuwait a pre-capita GDP of $22,800. The main imported items are food products, construction materials, vehicles and clothing (MOP, 2007).

Industry in Kuwait consists of several export-oriented petrochemical units, oil refineries, ammonia, fertilizers and cement. The labour force in Kuwait is about 2.2 million people, 1.87 million of which are non-Kuwaitis. Unemployment is relatively low compared with other Arab countries (MOP, 2007). There is no socioeconomic status hierarchy in Kuwait, which is a factor that is inversely related to the development of obesity (Coombs et al., 2013, Arauz Boudreau et al., 2013). Therefore, the development of obesity treatment intervention could potentially be affected by the lack of SES system where adherence to the intervention could be varied between participants as a result.

1.8.3 Education

Education is free and compulsory for all Kuwaitis until the age of 15 years. The system offers a number of different pathways to cater the varied needs of young people. From 2004-05 onwards, General education begins with Kindergarten (2 grades), progresses through Primary school (4 grades), Intermediate school (4 grades), and Secondary school (3grades); prior to 2004-05 each Primary, intermediate and secondary levels included 4 grades. The education system in Kuwait can be categorized between general education, vocational education, and other programmes of education. School canteens are present in all the government and private schools and are controlled by high committee and representatives from Ministries of Education, Health and Municipality. These bodies monitor the standards of foods sold and distributed yearly; however, what is allowed does not always represent healthy choices in terms of nutritious value (MOE, 2007).

1.8.4 Childhood obesity treatment initiatives in Kuwait

Although obesity screening and surveillance programmes have been taking place since the 1980’s at local and international levels as previously mentioned, with complete understanding of the growing problem of paediatric obesity, there has been no standard childhood obesity treatment manual or policy available in Kuwait to date. Furthermore, no clinical trials which attempted to treat paediatric obesity in Kuwait: it remains low priority in the public health agenda. The available regulations however encompass reception of motivated patients, of

varying age range, to the nutrition clinic in the Food and Nutrition Administration, taking the weight and height and using adult WHO cut off points for diagnosing obesity, taking a 24 hour food recall to estimate energy intake, and then finally using a set of 1200 kcal menus for each patient as a dietary plan. Furthermore, since the establishment of nutrition clinic in 1976, there has been no record of any audit carried out to evaluate the level of efficacy of the clinic. The filing system is collapsing with many patients having more than on file under their names, which adds more deficiencies for attempts of patients' follow up. Paediatric obesity epidemic in Kuwait has economic, educational, political and research dimensions which necessitate urgent detection and correction in order to avoid profound public health consequences.

Table 1.3 Population indicators

Indicator	Estimate		Unit	Reference period	Source
	Kuwaitis	Non-Kuwaitis			
Total population	1.1	2.5	million	2008	PACI
Annual population growth rate	2.7	3.8	%	2005	MOP
Crude Birth rate	33.9	15.1	%	2006	MOP
Population distribution by age:				2008	MOP
0-4 years	4	3	%		
5-14 years	7	5	%		
15-24 years	6	8	%		
25-59 years	11	50	%		
60+ years	1.5	1.5	%		
Population density	130.5		per Km^2	2003	MOP
Median age	30		years	2005	UNPD
Life expectancy at birth	78	n.a.	years	2003	MOP

n.a. : not available, Sources: Public Authority for Civil Information 2008 (PACI); Ministry of Planning, Central Statistical Office 2003, 2005, 2006 and 2008; and United Nations Population Development report 2005.

1.9 Thesis aims and research hypothesis

Choosing a treatment method for any disease in the population should firstly undergo the trial stage to assess its feasibility, efficacy for the short and long term, and whether or not this method is socially, culturally and gender appropriate. The available paediatric obesity treatment guidelines differ greatly between countries depending on the local health services structure, the available resources, culture and behaviours of the population. In the scope highlighted by the consensus from systematic reviews and guidelines, obesity treatment should aim at the entire family with the objective of changing dietary and physical activity and sedentary behaviour through resorting to intensive behavioural change and motivational techniques (NICE, 2013, SIGN, 2010, Oude Luttikhuis et al., 2009, McGovern et al., 2008). However, the style of delivering such treatment differs greatly in the literature and this could be divided into individual outpatient care or group-based programmes (de Mello et al., 2004). Medical literature reports only few studies on the treatment of paediatric obesity in group discussion fashion without the prescription of a diet and the results had been promising (Watson-Jarvis et al., 2011, Golan et al., 1998a, Braet et al., 1997b, Epstein et al., 1995b).

At baseline, at the recruitment stage we analysed the Health Related Quality of Life (HRQL) in a group of obese Kuwaiti adolescents and compared the results with healthy-weight peers (chapter 4). This was done using the Peds QL™ 4.0 generic questionnaire (Varni et al., 2001). It is now well established, from systematic review and meta-analysis, that obesity has a deleterious effect on the HRQL of children and adolescents from western societies (Ul-Haq et al., 2012, Griffiths et al., 2010). There is much less evidence on the extent to which obesity might impair HRQL in adolescents from other parts of the world: some degree of obesity-associated impairment of HRQL has emerged from studies of children or adolescents in Malaysia, Taiwan, and Lebanon (Lin et al., 2013, Lin et al., 2012, Hamzaid et al., 2011, Fazah et al., 2010). The primary purpose of the HRQL study was therefore to test the hypothesis that obesity is associated with impaired HRQL in Kuwaiti adolescents, as in western societies. A secondary aim was to test whether HRQL differed between self-reports and parent-proxy reports for the obese adolescents.

Chapter 5 describes the study on the prevalence of cardiometabolic risk factors in a sample of obese Kuwaiti adolescents (aged 10 to 14). We carried out assessments of obesity-related cardiometabolic risk factors that could impair vascular health and liver function. These included lipid profile (Cholesterol, LDL, VLDL, HDL, TG), IL-6, ICAM, CRP, adiponectin, liver function tests (ALT, AST, gGT) and insulin resistance by homeostasis model assessment

(HOMA-IR). The purpose of the study was to determine the prevalence of cardiometabolic risk factors and metabolic syndrome in a sample of obese Kuwaiti adolescents, as prevalence data might be helpful in improving engagement with obesity treatment in future.

Chapter 6 examines the feasibility of conducting a group therapy model in treating adolescent obesity in Kuwait (chapter 6). The National Adolescent Treatment Trial for Obesity (NATTO www.controlled-trials.com/ISRCTN37457227, Dec 1st 2009) is an RCT set out to compare a family-based behavioural treatment of paediatric obesity delivered in group discussion fashion with a primary care control.

2. General Methods

2.1 Introduction

This chapter outlines the design and methodology for chapters 4, 5 and 6. The National Adolescent Treatment Trial for Obesity (NATTO) intervention study (chapter 6) examined the feasibility and efficacy of family based behavioural treatment intervention for obese adolescents (intervention group) in Kuwait relative to a standard care (primary care control group, see chapter 1). NATTO was a single blinded randomised controlled trial aimed at adolescents aged 10 to 14 years. The methods and the treatment manual were based largely on systematic reviews, evidence-based guidelines and the Scotish Childhood Obesity Treatment Trial (SCOTT) (NICE, 2013, Hughes et al., 2008, Oude Luttikhuis et al., 2009, SIGN, 2010) (chapter 1). A full description of the treatment intervention and primary care control is described in chapter three. The intervention was delivered over a period of six months and the outcome measures were taken at baseline and six months. The trial used an intention to treat analysis and followed the CONSORT statement on the conduct and reporting of RCT (Boutron et al., 2008).

The research team wanted to answer the research question of whether a family based behavioural treatment programme for obese adolescents in Kuwait would be feasible and effective to treat obesity compared to primary care. The study's primary outcome was change in BMI Z score at 6 months. The study also aimed to investigate a number of secondary outcomes namely change in body fat, waist circumference and blood pressure. Beside these secondary outcomes, NATTO had two other outcomes for which only baseline assessments could be obtained (see chapter 7). These two outcomes were heallth related quality of life (chapter 4) and cardiometabolic risk factors (chapter 5). Therefore, these two studies are considered as separate studies and their methodologies are also described.

2.2 Health related quality of life study

The first phase of our research in Kuwait was to evaluate the association between health related quality of life (HRQL) and obesity in Kuwaiti adolescents aged 10 to 14 years. We wanted to test the hypothesis that with increasing body mass index (BMI), HRQL decreases. We compared HRQL of obese Kuwaiti adolescents with HRQL of healthy

weight Kuwaiti adolescents matched for age and sex. We also compared self-report HRQL of obese adolescents to their parent-proxy report.

2.2.1 Measurement of HRQL

The Pediatric Quality of Life Inventory (PedsQL ™ 4.0, MAPI Research Institute, Lyon, France) was used in the present study, with the Arabic Generic Version. The PedsQL™ is a generic HRQL questionnaire that has both self- and parent-proxy report forms (Varni et al., 2003). The forms are available in age-appropriate versions (5-7 years, 8-12 years and 13-18 years), and we used the version appropriate to the age of each study participant in the present study. The PedsQL ™ 4.0 is well-established, has been used most commonly in studies of child and adolescent obesity (Ul-Haq et al., 2012), and is a valid and reliable tool which is responsive to clinical change over time (Palermo et al., 2008, Varni et al., 2003). The Arabic Generic version of the PedsQL™ used in the present study is valid and reliable, e.g. with internal consistency for the different scales of 0.88-0.92 (Arabiat et al., 2011). The PedsQL™ measures a multidimensional construct that includes 23 items consisting of physical, emotional, social and school performance domains from which a total score, psychosocial score (composite of the emotional function, social function, and school function domains), and physical score are derived. Items are linearly transformed to a 0 to 100 scale, so that the higher the score, the better the HRQL.

2.2.2 Study participants

The sample was recruited from public (state) schools in Kuwait city, the capital of Kuwait. The original intention was to recruit adolescents from a random sample of public schools, but this proved not to be possible due to limited consent to participate from school headteachers. The Ministry of Education granted approval to the research team to invite all 80 intermediate schools in Kuwait City to participate in the study. Kuwait City has 41 male public intermediate schools and 39 female public intermediate schools. Only 10/80 intermediate school headteachers responded, from 3 girls schools and 7 boys schools, and of these 10, permission to conduct the study at school was granted by only three schools; two male and one female school. Participants and their families provided informed written consent. The PedsQL™4.0 Arabic version was completed independently by the adolescents at school and by their parents at home. The study was approved by the Medical Research Committee of the Ministry of Health and the Ethical Committee of the Ministry of Education in Kuwait.

Study participants were included if within the eligible age range (within grades 5-9, the grade range for intermediate schools, age 10 to 14y), and were either obese or healthy weight as defined below. Overweight pupils were excluded from the study sample in order to provide a marked contrast in weight status between the two groups of interest, and to minimize the impact of any mis-classification arising from use of the body mass index. Other exclusions were based on a brief medical history/checklist aimed at including only apparently healthy adolescents, and excluding participants with serious chronic or acute illness which might affect their HRQL.

2.2.3 Assessment of weight status and formation of obese-healthy weight matched pairs

A pre-planned paired analysis of HRQL between obese and healthy weight participants, with pair matching for same sex, same school, same school year, and same ethnic group (all participants were Kuwaiti nationals) yielded 98 pairs with 57 paired comparisons in boys and 41 paired comparisons in girls. More details in chapter 4.

2.2.4 Statistical analysis

All statistical analyses were performed using Minitab 16.0. Data were checked for normality. A full description of the study statistical analysis is given in chapter 4.

2.3 Cardiometabolic risk factors study

The main original intention of this present study was to measure cardiometabolic risk factors before and after initiation of a family-based obesity treatment intervention (NATTO) and to see if the treatment intervention had any positive impact on the measured cardiometabolic risk factors as clinical outcome. This original plan had to be altered and only baseline measures were taken (see chapter 7). The ethical approval for the thesis studies stated very clearly that permission was granted for baseline and end of trial blood collection. The head of the Laboratory Department at the Ministry of Health-Kuwait refused to grant the author permission to collect blood samples at 6 months (end of intervention) with the given reason that collection at that stage would require a new ethical approval from the Medical Research Committee-Ministry of Health-Kuwait, and the study supervisor (Professor John Reilly) would have to appeal directly to the head of the Laboratory Department in order to be granted permission to collect end of intervention blood samples.

In this study we carried out assessments of obesity-related cardiometabolic risk factors that could impair vascular health and liver function in obese adolescents. These included lipid profile (Cholesterol, LDL, VLDL, HDL, TG), IL-6, ICAM, CRP, adiponectin, liver function tests (ALT, AST, gGT) and insulin resistance (described in detail in the next section). To date, there are no published studies on the prevalence of these risk factors among Kuwaiti adolescents. The main aim of the study was to establish the prevalence of cardiometabolic risk factors in obese Kuwaiti adolescents, in order to establish whether such measures might be useful to encourage greater engagement with obesity treatment in future adolescent obesity treatment trials in Kuwait (chapter 5).

2.3.1 Study participants

Participants in the study were invited from among participants in the NATTO study (n=82). Eighty participants aged 10 to 14 years (40 males) consented and underwent a baseline clinical examination in 2009 and were diagnosed with obesity (BMI $\geq 95^{th}$ percentile for age and sex according to US CDC reference data). The participants had no other morbidities and were willing to provide blood samples for the current study. Participants and their parents signed an informed consent form. The study was approved by the Ethics Committee for Medical Research-Ministry of Health-Kuwait.

2.3.2 Blood sample collection and analysis

Participants underwent clinical examination including anthropometric assessment by the author. Blood sample collection was carried out by the author and it took place at 8 am in the outpatient clinic after an overnight fast (8-12 hours). Blood sample analysis was carried out by Dr Lynne Cherry of the Metabolic Medicine Group of the Cardiovascular and Medical Sciences division based at the BHF-GCRC Building at University of Glasgow. A full description of the study methodology is given in chapter 5.

2.4 The National Adolescent Treatment Trial for Obesity

The National Adolescent Treatment Trial for Obesity is an RCT set out to compare a family-based behavioural treatment of paediatric obesity delivered in group discussion fashion with a primary care control.

2.4.1 Ethical approval

NATTO study was granted ethical approval by the Ethics Committee for Medical Research-Ministry of Health-Kuwait. The research team in Kuwait consisted of a physician

(the author), a dietician, two assistant dieticians, and a waitress. All procedures were supervised by Professor John Reilly in Glasgow.

2.4.2 Study design

The trial was registered, conducted and reported in accordance with CONSORT guidelines (RCT Registered as National Adolescent Treatment Trial for Obesity in Kuwait (NATTO): www.controlled-trials.com/ISRCTN37457227, Dec 1st 2009) (Boutron et al., 2008).

2.4.3 Power calculation

No local data were available upon which to base a power calculation. The present study was therefore powered using BMI data from the Scottish SCOTT RCT (Hughes et al., 2008) which was used to develop the treatment intervention. NATTO treatment manual in essence was based on SCOTT treatment manual, with some modifications made to accommodate for group sessions.

Professor J H McColl (University of Glasgow-Department of Statistics) confirmed that with a between-group difference in the change in BMI Z-score of -0.25 at six months (which is a small change in BMI Z score) and a SD of change in BMI Z score of 0.21, giving a delta of 1.15, a sample size of around 30 adolescents per arm at 6 months would give 90% power at the 0.05 significance level. Dropout from the trial could not be predicted, but it was hoped that entering around 90 adolescents would make sufficient allowance for attrition during the 6-month study to leave around 30 participants per arm at the end of the trial. Of note, the MASCOT study which was and adaptation of SCOTT in Malaysia and was conducted at the same time of NATTO study in Kuwait, had a drop out rate of 26% at six months.

2.4.4 Delivery of treatment

The author and dietician delivered the treatment programme (chapter 3) to the intervention group. The sessions were carried out in the lecture theatre of Al Faiha polyclinic situated in Al Faiha area in the capital of Kuwait. The standard care was supposed to be delivered by the dieticians in the Central Nutrition Clinic of the Food and Nutrition Administration (FNA), Al Sabah Hospital in the capital, which was considered a primary care level for the treatment of obesity. Care was taken to avoid contamination between the two treatment groups. Both the author and dietician worked solely with the intervention group and did not attend the FNA at any stage during the conduct of the trial. The author and dietician

were also aware of the importance of not discussing any aspect of the intervention programme with the standard care dieticians.
The schools and residences of all participants were located in the capital, and both the venue for the intervention (Al Faiha polyclinic) and the venue for the control primary care clinic were also in the capital, just to ensure that distance was not an issue hindering attendance

2.4.4.1 Intervention

The intervention was originally intended as a relatively moderate intensity (12 sessions biweekly with 12 hours contact time, delivered in group discussion fashion) programme, delivered over 6 months period largely by the author who led every session (more details in chapter 3). However, attendance at the second and third sessions was poor and modification to the sessions' scheduling had to be made to ensure better attendance, therefore, the intervention was altered to low intensity programme by having one session every month for 6 months.
There were 2 groups, one for girls and one for boys, each consisting of the parents (at least one parent) and their adolescents.
The primary aim of the intervention was modification of lifestyle which would slightly reduce BMI Z score (Danielsson et al., 2012, Weigel et al., 2008).

2.4.4.2 Control

The control group agreed to seek the available standard care from the Food and Nutrition Administration clinic and was given the clinic phone numbers to arrange for appointments. This was considered a primary care level for the treatment of paediatric obesity in Kuwait. It is based on clinical assessment by the clinic physician, then a referral to the clinic dietician where the patient would be given a set menu of 1200 Kcal diet and an appointment in two weeks for follow up. None of the families attended primary care (chapter 6).

2.4.5 Inclusion and exclusion criteria

The study enrolled adolescents of intermediate school age, 10 to 14 years old, who were clinically obese as defined by the US CDC 2000 definition of BMI $\geq$ 95centile (Kuczmarski et al., 2000) and whose parents were willing to participate in the study. Diagnosing obesity was based on BMI CDC reference data and cut off points in the current thesis as the local reference data were proved to be rather inaccurate (El-Ghaziri et al.,

2011). Moreover, BMI as an index of obesity correlates well with body fatness, morbidity and mortality (Cole et al., 2005).

At least one parent was required to attend the treatment sessions. Adolescents were eligible for inclusion if they satisfied the inclusion criteria;

- Aged between 10 to 14 years old.
- Had BMI $\geq 95^{th}$ centile (US CDC reference).
- Had no obvious underlying medical cause of obesity.
- Had no serious co-morbid conditions requiring medical or surgical attention.
- Were attending main stream schools (public schools).
- Had not received any weight loss management in the past 12 months.
- Were of Kuwaiti nationality.

Participants were excluded if they:

- Were diagnosed with obesity as part of a medical condition or due to drug therapy.
- Had serious medical or surgical co-morbidities.
- Were receiving weight management therapy.
- Were not Kuwaiti nationals.

2.4.6 Recruitment

The recruitment process took place from September until November 2009. A list of public intermediate schools in the capital of Kuwait was obtained from the Ministry of Health, updated for the year 2009. There were a total of 41 male and 39 female public schools in the capital of Kuwait. The author made phone calls to these 80 schools explaining the nature of research and the likelihood of their participation after random selection. Only 10 schools agreed to grant the research team access to their premises. The research team consisting of the author and the two assistant dieticians visited these 10 schools and only 3 (2 male and 1 female schools) were willing to take part in the study. Therefore random school sampling as intended originally was not possible under the circumstances.

The first phase of the study was in the form of BMI screening to identify for eligibility; obese, overweight and healthy weight adolescents (aged 10 to 14 years old).

Screening started by the assistant dieticians visiting every classroom from grade 5 to grade 9 in every school, taking the weight and height measurements as described in section **2.2.11 Outcome measures**, and assessing students for eligibility using a check list present in all forms used for recording the results (appendix1). Potentially suitable subjects' measurements were plotted by the author using age appropriate gender specific BMI charts

(Kuczmarski et al., 2000). Participants were categorised into healthy weight (BMI ≥5rd centile and <85th centile of US CDC reference population), obese (BMI ≥95th centile of US CDC reference population) and ineligible group (where overweight was defined as BMI ≥85th centile and <95th centile of US CDC reference population, or those who were obese but did not fit the inclusion criteria). This yielded 224 potentially eligible obese students (142 males or 63%) and 276 healthy weight pupils (176males or 63%). The total number of excluded students was 542 which included overweight students (n=536) and 6 obese students who did not meet the inclusion criteria. At this stage, all obese and healthy weight students were assigned a unique study code and participated in health related quality of life study comparing health related quality of life between obese and healthy weight Kuwaiti adolescents (see section **2.3**).

2.4.7 Consent

The entire obese group was given consent forms explaining the nature of the trial in details, as directed by the Ethical Committee of the Ministry of Health in Kuwait. Any willing family had to sign the consent forms attached to each information sheet (appendix 1), one for the participating parent and one for the participating adolescent. Collection of the information and consent package was done by the author from the adolescents in the schools. We aimed to collect more than 100 consent forms of families agreeing to participate in the study; however, we got 91 forms back of families willing to participate, 44 of adolescent boys and 47 of adolescent girls.

Each eligible and willing adolescent was invited with at least one parent to come to the nutrition clinic where the author carried out a thorough history and clinical examination, and baseline measurements were taken including weight, height, and waist circumference. At this point, the study was explained in detail to the parent and the adolescent.

If families were allocated to the intervention group, the author then sent them the intervention programme timetable and made phone calls two days prior to each session to confirm attendance. In addition, all parents and adolescents were assured that withdrawal at any stage of the programme is permissible without any consequences.

2.4.8 Randomisation and concealment

Prior to random allocation, all obese adolescents were assigned a unique study code at the baseline assessment stage (section **2.2.6 Recruitment**). The 91 eligible and consented adolescents and their parents were invited to the nutrition clinic for full physical examination, blood sampling, and basic anthropometric measurements. Nine of the invited

families failed to show up for their appointments after repeated rearrangements of their appointments. The remaining 82 participating adolescents consisted of 42 boys and 40 girls. Their study codes were sent electronically to the team's statistician Professor John McColl at University of Glasgow who then produced a computer generated stratified randomisation list assigning the participants to either the intervention group (n=41) or to the control group (n=41). The list was sent electronically to the author who in turn informed the participants of their assignment by phone calls. The study timetable was delivered by the author to the adolescents of the intervention group in their schools.

2.4.9 Blinding

All the baseline anthropometric measurements were taken before group allocation by the assistant dieticians. At six months, all anthropometric measurements were taken by the same assistant dieticians who were not involved in the delivery of either the intervention or the standard care. They work in a different sector of the FNA and hence had no contact with the author, the participants or their families throughout the study.

2.4.10 Retention

Participants' retention in paediatric weight management studies ranged from 0 to 41% as summaised in the most recent Cochrane review (Oude Luttikhuis et al., 2009). Poor retention rates have serious implications for the intention to treat analysis and can result in the study being underpowered, so every effort was taken to limit attrition. This was done by rescheduling of intervention sessions' date and time to suit the intervention group.
The treatment intervention was delivered in group discussion fashion, and hence the author reminded the parents of their appointments before every session by means of phone calls and short messaging services (SMS). Families were expected to attend 12 sessions over 6 months period (two sessions every month). However, due to poor attendance record after the third session, the sessions were condensed to 6 sessions (one session every month) for practicality. The author also kept an attendance record for all the sessions.

2.4.11 Outcome measurements

The primary outcome measure for the study was change in BMI Z score. BMI Z score is commonly used in obesity intervention trials as an outcome measure because it is believed to be the best measure to assess fat mass change over time (Ford et al., 2010, Hunt et al., 2007, Cole et al., 2005).

Secondary outcome measures consisted of estimated change in body fat, waist circumference and blood pressure.
At Baseline, the author collected blood samples from each eligible subject as part of an assessment of cardiometabolic risk factors. The intention was to measure these risk factors before and after the intervention (end of trial). However, end of trial assessment of cardiometabolic risk factors in obese Kuwaiti adolescents was faced with opposition from the head of the laboratory department in the Ministry of Health-Kuwait. Therefore, NATTO end of trial outcomes did not include cardiometabolic risk factors profile.

Measurements of height, weight, percentage body fat and waist circumference were taken by the team's two assistant dieticians at baseline (at baseline clinic assessment) and six months after the first clinic assessment in the schools. As mentioned, both of the assistant dieticians work in a different sector of the FNA, involved in the yearly Kuwait National Surveillance System (KNSS) produced by FNA, hence, the assistant dieticians remained blinded to group allocation throughout the study and until after the six-months study data were collected. The team's assistant dieticians receive yearly training in all the necessary measurement techniques from the Food and Nutrition Administration and followed standard written protocols for the measurements, as part of their work done in relation to the KNSS.

BMI Z score, height, weight, and body fat

The heights of the subjects were measured using Leicester height measure (Chasmors, London, United Kingdom). The subject was measured with socks and shoes removed, standing upright and barefoot with feet together in the centre of the base plate. Height (m) was measured to the nearest 0.1 cm.

The subject's weight was measured using Tanita electronic scale model TBF-300 (Chasmors, London, United Kingdom), with subjects in light clothing without shoes. This same machine was used to estimate percentage body fat. Weight (kg) was measured to the nearest 0.1 kg.

Bioelectrical impedance is a clinically useful, convenient and relatively cheap method to assess body composition, which has become more popular in recent years both in clinical settings and research (Hunt et al., 2007, Kyle et al., 2004, Sung et al., 2001). The machine measures the resistance (impedance) to a low level electric current travelling through body

tissues. Although the estimated body fat produced by the device is specific to the model of the BIA used (Kyle et al., 2004), it still provides a useful information on the change in percentage body fat over time in response to treatment intervention (Sung et al., 2001).

Values of height and weight were used to calculate BMI (kg/m²) values. BMI Z scores were extracted using BMI, decimal age and gender and SAS Programme to calculate z score for US CDC (http://www.cdc.gov/nccdphp/dnpao/growthcharts/resources/sas.htm). The primary study outcome measure was BMI Z score calculated relative to US CDC 2000 BMI for age reference data (Kuczmarski et al., 2000). In a study by Al-Isa and Thalib in 2008 (Al-Isa and Thalib, 2008) to produce a local reference data for BMI of Kuwaiti adolescents aged 10 to 14 years, the authors compared local BMI reference percentiles with US CDC BMI reference percentiles. The local BMI percentiles cut off points were shifted to higher level than that of the US CDC level, possibly due to the high prevalence of adolescent obesity in Kuwait that might had contributed to this shift (El-Ghaziri et al., 2011). Therefore, we decided to use US CDC BMI reference percentiles in NATTO. In addition, US CDC BMI cut off point for obesity is strong predictor of cardiometabolic risk factors and insulin resistance in young adulthood (Harrington et al., 2013).

Waist circumference

Waist circumference was measured using a flexible, inelastic tape measure (Supralip® 160, West-Germany). The waist circumference was measured on the horizontal plane 4 cm above the umbilicus with the abdominal muscles relaxed and the subject breathing shallowly (Rudolf et al., 2007). Waist circumference is a measure of central fat mass (visceral fat) that cotributes to the development of impaired lipid profile, high blood pressure and metabolic complications (Haas et al., 2011, Reilly et al., 2010, Hirschler et al., 2005, McCarthy et al., 2005). Although not superior to BMI for the diagnosis of obesity (Reilly et al., 2010), we chose to include waist circumference as a secondary outcome to be part of the cardiometabolic risk factors (Watts et al., 2008) that were supposed to be assessed at baseline and end of trial (section **2.3**).

Blood Pressure

Blood pressure was measured in all participating adolescents during the first clinical assessment visit using a desk mercury sphygmomanometer (diplomat-presameter, Reister, Germany). The measurement was performed by the author. In daily life, blood pressure changes from instant to instant and is influenced by many physiological and environmental

factors. The subjects were seated comfortably on a chair for at least 5 minutes prior to blood pressure measurement. A set of 2 different size cuffs were present to ensure proper selection of the cuff size, ideally covering two thirds of the subject's upper arm. The blood pressure measurement was repeated three time and the average of the three readings was recorded (Bird and Michie, 2008, NHBPEP, 2004). Blood pressure is considered one of the modifiable cardiovascular risk factors in adults and adolescents (Anyaegbu and Dharnidharka, 2014). Obese children and adolescents are more likely to develop hypertension than their healthy weight peers (Herouvi et al., 2013). Sometimes with BMI Z score reduction of 0.5 improvement in blood pressure profile of obese children and adolescents could be reached (Danielsson et al., 2012, Reinehr and Andler, 2004). Measuring blood pressure in the present study was intended to be part of the cardiometabolic risk factor assessment before and after the intervention. As with waist circumference, baseline and end of intervention assessment where obtained but not for the blood based other cardiometabolic risk factors.

2.4.12 Data analysis

Data were analysed using Minitab 16. For the purpose of this thesis, an intention to treat analysis was conducted. This refers to the process of analysing data for each subject in the groups they were allocated and no subjects were removed from the analyses by the author. The analysis used all the available data for each group, regardless of their adherence to the protocol, i.e. compliance. If a family failed to attend 50% of the sessions, they were considered to be non-completers of treatment. All subjects were analysed within the groups to which they were randomly allocated, i.e. intention to treat analyses. A full description of the statistical analysis is given in chapter 6.

In summary, the study with the largest sample size was the HRQL study (details in chapter 4) from which only 82 consented to participate in the NATTO study (details in chapter 6), and from those 82 participants, 80 participants consented for blood sample collection (details in chapter 5).

3. Development and Description of the NATTO Treatment Manual

3.1 Introduction

As described in chapter1, a large body of evidence suggests the need for dietary therapy, increased physical activity, and decreased sedentary behaviour through behaviour modification techniques for the success of any child or adolescent obesity treatment intervention as summarised in the recent systematic reviews and evidence-based guidelines (NICE, 2013, SIGN, 2010, Oude Luttikhuis et al., 2009, Hughes and Reilly, 2008, McGovern et al., 2008, Barlow, 2007). The NATTO treatment programme was therefore based on these principles. Weight management requires conscious effort and readiness to change, accompanied by the adequate knowledge and education concerning how to improve dietary and physical activity/sedentary behaviours for the improvement of health status in the long term. However, the recent systematic reviews and clinical guidelines (NICE, 2013, SIGN, 2010, Oude Luttikhuis et al., 2009) fell short of providing the mechanisms by which these behaviour modification techniques should be delivered, and indicate in general terms that behavioural modification techniques should be used to achieve the changes, but do not provide practical details as to how treatment programmes should be developed. Well described, evidence-based, simple and readily generalisable childhood obesity treatment interventions are still scarce in the literature, and there is no consensus on what really works in terms of treating adolescent obesity (Danielsson et al., 2012, Hughes et al., 2008, Stewart et al., 2005). Furthermore, there is still a gap between regions of the world in research done to test the effectiveness of treatment interventions for paediatric obesity (Oude Luttikhuis et al., 2009). As noted in chapter 1, nearly all previous paediatric obesity treatment trials were from the USA or Europe. The author's most recent literature search in PubMed in 2013 also found no paediatric obesity treatment trials done in the Arabian Gulf region or the Middle East. In addition, if any future obesity treatment research is to be built on existing research, it is important to describe what was done in the existing research in detail. The present chapter therefore aims to describe the NATTO treatment programme in detail.

3.2 SCOTT (Scottish Childhood Obesity Treatment Trial)

The SCOTT study was a randomised controlled trial of a best practice behavioural programme for treatment of childhood obesity. It involved 134 obese children of primary school age (5-11 years old) randomised to either the intervention group or the standard care group in Glasgow and Edinburgh, Scotland (Hughes et al., 2008). The intervention used individualised dietetic treatment sessions (8 sessions) over a period of 6 months. The intervention was basically a family-centred behavioural change technique influenced by the work of Epstein's group, which used a modified version of the traffic light diet scheme, self-monitoring, goal setting and relapse prevention applied to diet, physical activity, and sedentary behaviour (Stewart et al., 2005, Epstein, 1996, Epstein et al., 1998). The author of this thesis received an intensive five-days training course on the SCOTT programme.

Choosing the SCOTT programme as the basis of the NATTO treatment was based on several points. Firstly, it was a family centred intervention focused on changing the behaviours recommended as the key targets in recent evidence based management guidelines (NICE, 2013, SIGN, 2010, Oude Luttikhuis et al., 2009) for the treatment of paediatric obesity (reduction in sedentary behaviour, particularly screen-media use; diet, using a modified version of the 'traffic light diet' system (Hughes et al., 2008); and promotion of physical activity). Second, the intervention incorporated theoretically based behaviour change techniques to all three of the targeted behaviours based on the theory of planned behaviour and social cognitive behaviour (Hughes et al., 2008): exploration of the pros and cons of changes in diet, physical activity, and sedentary behaviour; exploration of motivation to change diet, physical activity, and sedentary behaviour; self-monitoring of sedentary behaviour (recording of screen time in diaries), diet, and physical activity (recording of walking, sport, and physically active play in a diary); identifying the main barriers to behaviour change and problem solving in relation to these barriers; goal setting in relation to diet, physical activity, and sedentary behaviour; relapse prevention. Thirdly, SCOTT programme was available to the author and that was the starting point.

3.3 The rationale for using group setting in NATTO intervention programme

The development of wide-reaching, effective strategies for the treatment of paediatric obesity are necessary. Studies on the effectiveness of group based programmes are promising (Garipagaoglu et al., 2009, Weigel et al., 2008, Kalavainen et al., 2007). In Garipagaoglu and colleagues study, group treatment was superior to individualised standard care in reducing BMI Z score during the intervention period (3 months) and

participants maintained that decline at 1 year follow up (Garipagaoglu et al., 2009). Weigel et al (2008) tested a 1 year group treatment programme for paediatric obesity (participants' age 7 to 15 years) against outpatient care and showed significant decrease in BMI Z score, systolic blood pressure and fat mass in the intervention group (Weigel et al., 2008). Similar results were obtained by Kalavainen and colleagues (2007) in a randomised controlled trial of a group intervention programme versus routine individual counselling (Kalavainen et al., 2007). In another study, de Mello and colleagues suggested that group therapy could be an appropriate alternative to individual counselling (de Mello et al., 2004), especially because when choosing group treatment the cost-effectiveness is more than that of the individualised treatment (Goldfield et al., 2001). In the light of the mentioned advantages, we choose group treatment for NATTO for its potential clinical as well as cost-effectiveness. Some evidence suggests that approaching families in group fashion might enhances participation, adherence and facilitate cohesion (Martin et al., 2009).

3.4 Components of the NATTO treatment manual

3.4.1 The structure of the NATTO treatment programme

Our NATTO treatment programme focused on family involvement and on bringing about long term lifestyle changes. Based on the different content sources mentioned earlier, the NATTO treatment programme was a relatively low intensity programme with the aim of making it more generalisable and less demanding. It was felt that a one hour session every month for the length of the six months treatment programme, one for males and their parents, and one for females and their parents, either on the same day or on separate days, would provide enough contact time with the participants to deliver the programme and also to assess participants' compliance. Each session was given by the author and the team's dietician, previously trained as to the mode and method of delivery. The lectures were prepared by the author together with the head supervisor Professor John Reilly, and used a practical approach. After each session, the groups participated in reviewing the session attended and their commitment to the previous session. Any questions, concerns and suggestions were welcomed at that stage, from both parents and adolescents. Healthy snacks in the form of fruits or vegetables were offered at the end.

The NATTO sessions included nutrition education, physical activity and behaviour modification topics delivered by the physician (author) and a dietician. The participants were provided with treatment handouts that were modified from SCOTT materials

(Stewart et al., 2005) supplemented with additional self-developed material (Appendix1). The content of each session in the NATTO treatment programme is outlined in Table 3.1.

The sessions were held in a lecture theatre in Al Faiha polyclinic, an area of central location in the capital Kuwait City. Parents and adolescents were reminded of each session one week, two days and one day before by SMS sent by the author. Sessions were held separately for males and females as mentioned above, to comply with the Kuwaiti culture of gender segregation.

3.4.2 Family involvement in the NATTO intervention programme

There were three lifestyle behaviours that were the main targets for change in the NATTO treatment programme. These targets were recommended by recent systematic reviews (Oude Luttikhuis et al., 2009, McGovern et al., 2008, Barlow, 2007) and clinical guidelines (NICE, 2013, SIGN, 2010) : dietary modification, physical activity and sedentary behaviour. Behavioural modifications in the NATTO treatment programme were directed mainly at the obese adolescent; however, for any change to take effect it should involve the parents for their help and supervision, so treatment efforts in NATTO were meant to involve the entire family, as it is strongly recommended by NICE 2013 and SIGN 2010 guidelines. The work of Golan and colleagues (Golan et al., 1998a, Golan et al., 1998b) is of particular interest as they have lead this field and devised a theoretical method for childhood obesity treatment emphasising the role of parents as the primary agents for change in the treatment process. They concluded that changing the socio-ecological context of the family i.e., modifying the home environment, providing healthful role modelling, developing family targets related to physical activity and healthful eating, targeting family change rather than child-centred change, and adapting health-centred rather than weight-centred approach, is most likely to produce a significant and clinically meaningful BMI Z score reduction in obese children (Golan and Weizman, 2001).

Table 3.1 Components of the NATTO treatment programme

Session	Topic	Contents	Behaviour change techniques	Next appointment
1	It's your life	Obesity complications The pros and cons of obesity treatment How to start!	Goal setting, contracting and rewards, Self-monitoring	in 2 weeks
2	Eat well	Energy balance Modified traffic light diet Food reference guide	Goal setting, contracting and rewards, Self-monitoring	in 4 weeks
3	Enjoy living	How to increase physical activity How to decrease sedentary behaviour	Goal setting, contracting and rewards, Self-monitoring	in 4 weeks
4	Summer fun	Tips on meal choices Cooking together healthly		in 4 weeks
5	Take it easy	Dealing with tricky situations Dealing with relapse	Problem solving relapse prevention	in 4 weeks
6	NATTO forever	Family stories Sharing tips Long term goals	Goal setting, contracting and rewards, Self-monitoring	

3.4.3 Dietary component

Adapted from the SCOTT novel dietetic treatment, the dietary component in NATTO composed mainly of the modified traffic light diet (Stewart et al., 2005). The modified traffic light diet is a simplified, less complex version of the traffic light diet proper established by Epstein and colleagues(Epstein et al., 1998). It classifies energy dense, high fat and high sugar foods in the red zone, fruits and vegetables in the green zone, and starch, meat and dairy foods in the amber zone. The anxiety of calorie counting has been omitted in this version which puts the parents and their children in a less stressful situation. However, the ultimate goal after 6 months of therapy is to restrict the intake of red foods to one per day, restrict intake of amber foods to meal times and green foods to be taken freely and substituted for red foods. Emphasis was also put on the method of cooking and avoidance of frying and using ready-made high fat high sugar content products such as sauces and pastes. These recommendations made up the dietetic part of the group sessions to convey the healthy eating message. Simple dietetic aids, illustrations and practical were used in the sessions to demonstrate portion sizes, calorie contents, and fat contents only to give an example and to extend the participants' knowledge on what they are eating without rigidly applying this intensive information into their modified dietary habits. Examples of healthy local food alternatives to energy dense food choices were also demonstrated.

3.4.4 Sedentary behaviour and physical activity

Increasing physical activity and decreasing sedentary patterns are an essential part of any obesity treatment programme as noted above (Oude Luttikhuis et al., 2009, SIGN, 2010). Increasing the level of physical activity in childhood and adolescence increases bone density, decreases obesity and decrease the risk of developing of cardiovascular disease risk factors (O'Donovan et al., 2010). The current evidence-based guidelines recommend that all children and adolescents aged 6 to 17 years accumulate at least 60 minutes of moderate to vigorous intensity physical activity per day (SIGN, 2010, O'Donovan et al., 2010, NICE, 2013, Strong et al., 2005). This involves structured and non-structured physical activity. The approach should be incremental allowing for the individual's capacity to perform these activities and to avoid injury. Moderate intensity physical activity is when one notices an increase in the heart rate and respiratory rate to 5 or 6 in a scale of 1 to 10, and vigorous intensity physical activity is when the individual feels the heart and respiratory rates reach up to 7 or 8 (Landry and Driscoll, 2012).

Sedentary behaviour or physical inactivity is also targeted as behaviour distinct from physical activity. Controlling sedentary behaviour e.g. TV viewing, is sometimes seen as a more practical and realistic goal in treating obesity (Landry and Driscoll, 2012, Ortega et al., 2008, Reilly and McDowell, 2003) than targeting physical activity. In fact, targeting sedentary behaviours have been associated with a significant reduction in overweight and can lead to an increase in physical activities (O'Donovan et al., 2010, Epstein et al., 1995b). For the long term, decreasing sedentary behaviour can be sustained more effectively than when targeting an increase in physical activity (Epstein et al., 1998). The current recommendations conveys that sedentary behaviour should be reduced to a maximum of 2 hours per day (NICE, 2013, SIGN, 2010).

In NATTO we used a culture-sensitive approach in delivering the treatment recommendation for reducing sedentary behaviour especially screen time and increasing the level of physical activity (e.g. using the stairs and helping in house chores) and indoors physical activities and encourage active play. The ultimate goal was to get the participants to be active on regular basis in any fun, safe and enjoyable activity. In Kuwait, a lack of exercise facilities especially for females is one of the factors attributed to decreased physical activity among adolescents (Al-Isa et al., 2011), as well as the weather, which is mostly extremely hot most time of the year. In our programme we tried to explore ways for the participants to be more physically active in a way that could be sustained for life. Play with family members and friends was repeatedly suggested by the participants in each session.

We also emphasised the role of the parents as role models in leading active lifestyle and in supporting their children's participation in enjoyable physical activity.

3.4.5 Behaviour change techniques

As mentioned above, managing obesity in childhood and adolescent is done through changing behaviour towards diet, physical activity and sedentary behaviour usually by means of multiple, intertwined methods of changing behaviour, or behaviour change techniques (BCT) (NICE, 2013). Using these techniques in childhood and adolescent obesity treatment interventions has been proven to be effective in the short and long term (Epstein et al., 1994, Wilfley et al., 2007, Golan et al., 1998a, Robinson, 1999). Abraham and Michie (2008) developed a taxonomy of 26 conceptually distinct component BCTs, which are described using consistent terminology and standard definitions (Abraham and Michie, 2008)(Table 3.2). More recently, the original taxonomy (Abraham and Michie,

2008) has been revised and extended into a behaviour-specific taxonomy of 40 BCTs for physical activity and healthy eating behaviours (CALO-RE) (Michie et al., 2011). The CALO-RE taxonomy was developed by three teams of researchers from Coventry, Aberdeen and London to provide standard definitions to reliably identify techniques used for (1) increasing physical activity and healthy eating primarily in obese adults and (2) increasing self-efficacy to promote lifestyle and recreational physical activity. There is still uncertainty about how to match BCT to theoretical constructs and more research is needed to discover the theoretical basis (Michie et al., 2011), however, having the taxonomy implemented in intervention protocols facilitated the scientific investigation of behavioural interventions, which would allow for the replication of effective interventions as well as intervention evaluation (Michie et al., 2008).

Our intervention programme employed a number of behaviour change techniques in order to help the participants and their parents understand the health consequences of obesity as a result of their current lifestyle, encourage them forming goals and specific plans to initiate change, help them develop strategies to cope with difficult situations where relapse is possible. The behaviour change techniques used in NATTO consisted of goal setting, self-monitoring, rewards and contracting, stimulus control, problem-solving and relapse prevention (Abraham and Michie, 2008). These techniques are described briefly below.

Table 3.2 Definitions of 26 Behaviour Change Techniques and Illustrative Theoretical Frameworks

Technique	Definition
1. Provide information about behaviour-health link	General information about behavioural risk, for example susceptibility to poor health outcomes or mortality risk in relation to the behaviour
2. Provide information on consequences	information about the benefits and costs of action or inaction, focusing on what will happen if the person does or does not perform the behaviour
3. Provide information about others' approval	Information about what others think about the person's behaviour and whether others will approve or disapprove of any proposed behaviour change
4. Prompt intention information	encouraging the person to decide to act or set a general goal to make a behavioural resolution
5. Prompt barrier identification	Identify barriers to performing the behaviour and plan ways of overcoming them
6. Provide general encouragement	Praising or rewarding the person for effort or performance without this being contingent on specified behaviours or standards of performance
7. Set graded tasks	Set easy tasks, and increase difficulty until target behaviour is performed
8. Provide instruction	Telling the person how to perform a behaviour and/or preparatory behaviours
9. Model or demonstrate the behaviour	An expert shows the person how to correctly perform a behaviour, for example, in class or on video
10. Prompt specific goal setting	Involves detailed planning of what the person will do, including a definition of the behaviour specifying frequency, intensity, or duration and specification of at least one context, that is, where, when, how, or with whom
11. Prompt review of behavioural goals	Review and/or reconsideration of previously set goals or intentions
12. Prompt self-monitoring of behaviour	The person is asked to keep a record of specified behaviour(s) (e.g., in a diary)
13. Provide feedback on performance	Providing data about recorded behaviour or evaluating performance in relation to to a set standard or others' performance, i.e., the person received feedback on their behaviour
14. Provide contingent rewards	Praise, encouragement, or material rewards that are explicitly linked to the achievement of specified behaviour
15. Teach to use prompts or cues	Teach the person to identify environmental cues that can be used to remind them to perform a behaviour including times of day or elements of contexts
16. Agree on behavioural contract	Agreement (e.g., signing) of a contract specifying behaviour to be performed so that there is a written record of the person's resolution witnessed by another
17. Prompt practice	Prompt the person to rehearse and repeat the behaviour or preparatory behaviours
18. Use follow-up prompts	Contacting the person again after the main part of the intervention is complete
19. Provide opportunities for social comparison	Facilitate observation of nonexpert others' performance for example, in a group class or using video or case study
20. Plan social support or social change	Prompting consideration of how others could change their behaviour to offer the person help or (instrumental) social support and/or providing social support
21. Prompt identification as a role model	Indicating how the person may be an example to others and influence their behaviour or provide an opportunity for the person to set a good example
22. Prompt self-talk	Encourage use of self-instruction and self-encouragement (aloud or silently)

	to support action
23. Relapse prevention	Following initial change, help identify situations likely to result in readopting risk behaviours or failure to maintain new behaviours and help the person plan to avoid or manage these situations
24. Stress management	May involve a variety of specific techniques (e.g., progressive relaxation) that do not target the behaviour but seek to reduce anxiety and stress
25. Motivational interviewing	Prompting the person to provide self-motivating statements and evaluations of their own behaviour to minimize resistance to change
26. Time management	Helping the person make time for the behaviour (e.g., to fit it into a daily schedule)

Adapted from Abraham and Michie 2008

Goal setting

The adolescent is given the responsibility to identify a certain behaviour or set of behaviours that he/she wishes to change. The role of the author was to make sure that this goal or goals are SMART, i.e.; Small, Measurable, Achievable, Recorded and Timed (Stark, 2003, Stewart et al., 2008b), and personal, i.e.; targeting the participant's own lifestyle behaviour(s) that he/she thinks need to be changed. Although the adolescent chose the lifestyle behaviour he/she wished to change, the parent(s) also were asked to provide their help and support for their child in order to: identify the targeted behaviour(s) for change at a particular time point, keep their child motivated in pursuing change in behaviour, identify with their child ways for achieving and maintaining such change in behaviour. The participants were asked to set a maximum of three behaviour change goals to achieve by the end of the programme.

Self-monitoring

Self- monitoring involved keeping a record of the participant's dietary intake and physical activity behaviour. In the NATTO treatment programme, we distributed self-monitoring diaries aided with dietary and physical activity tips and illustrations (appendix1), to be used by all participants for them to reflect on their targeted behaviour(s) and to also record any events that either helped them reach and maintain their targeted change in behaviour or posed a threat in their process of changing the behaviour. This method enhances attention to one's actions and the surrounding environment (Stark, 2003, Burke et al., 2011).

Contracting and rewards

The use of contracting between the participant and the parent with the supervision of the author was very essential reinforcement of the goal setting and the self-monitoring steps mentioned above. Signing a contract meant that both the parent and the participant agreed

on the set goals to be achieved within the decided time frame and that both had the responsibility of monitoring the process of achievement. Decision on the reward was based on achieving 100% of the set goals and the actual reward was a non-food item, inexpensive and preferably involved a family function. At the end of the NATTO intervention programme, parents and their children were asked to set new goals and to sign a new contract.

Stimulus control

The context in which the challenging behaviour is occurring is altered using stimulus control. Modifying the surrounding environment is a way of controlling the obesity augmenting behaviour, and promoting new lifestyle changes that help the participant achieve the behavioural goals. Stimulus control and the corresponding environmental modifications can be used by parents to reduce the repetitive behaviours that contributed to obesity and allows the participants to engage in the new 'appropriate' behaviour more quickly. For example, reduce buying red foods, or encouraging physical play with family members.

Problem solving

To overcome difficult situation where sticking to goals could be compromised, the participants and the parent were encouraged to identify high risk situations and access the possible ways to overcome the situation. In NATTO, both parents and their children were asked to give examples from their personal experience about situations that could be labeled as high risk and also to give more than one solution to the problem at hand.

Relapse prevention

In order to prevent relapse into the unwanted behaviour, it is crucial to explore the participants' and their parents' believes regarding obesity and its consequences. Correcting or even expanding on the person's believes towards obesity and its link to the unwanted behaviour help the participant cope with relapse situations, and also reflect on their goal setting and stimulus control strategies. This also helps the participant to plan ahead for difficult situations.

More recent evidence suggests the use of other behaviour change techniques that carry more potentially successful outcomes (Martin et al., 2013) (see chapter 7).

3.5 Primary care control treatment

At the start of this trial, the author and the trial supervisor felt that it was essential to compare the NATTO programme to the standard dietetic care that was delivered in Kuwait at primary level (**see chapter 1**). There was no formal training in childhood obesity treatment at primary or secondary care levels in Kuwait. The central nutrition clinic offers weight management walk in service to the public regardless of age and is considered a primary care centre. The patient gets his/her anthropometry measured at first contact, along with blood samples for complete blood count (CBC), liver function test (LFT), renal function test (RFT), fasting blood glucose (FBG) and lipid profile. The next appointment is usually held in 2-3 weeks, where the patient firstly meets the clinic physician for full system screening and then sits with the clinic dietician for dietary management. The dietary management is composed of a diet sheet/menu and usually the patient is followed by the same dietician monthly thereafter.

4. Obesity and Health Related Quality of Life among Adolescents in Kuwait

BOODAI, S. A. & REILLY, J. J. 2013. Health related quality of life of obese adolescents in Kuwait. *BMC Pediatr,* 13**,** 105. Appendix E.

4.1 Introduction

In clinical settings, measures of Health Related Quality of Life (HRQL) are not routinely explored using conventional history taking and physical examination. However, poor obesity-associated quality of life might lead adolescents and/or their families to seek professional treatment of obesity. The effects of obesity in youth on HRQL have been characterised mainly from the Western World to date (Griffiths et al., 2010). There is much less evidence on the extent to which obesity might impair HRQL in adolescents from non-western societies(Lin et al., 2013, Lin et al., 2012, Hamzaid et al., 2011, Fazah et al., 2010, Chen et al., 2005), but obesity-associated impairment of HRQL has emerged in children, adolescents, and young adults in Malaysia, Taiwan, and Lebanon (Lin et al., 2013, Hamzaid et al., 2011, Fazah et al., 2010, Chen et al., 2005).

In a recent systematic review (Griffiths et al., 2010) and a recent meta-analysis (Ul-Haq et al., 2012) of the association between body mass index (BMI) and health-related quality of life among children and adolescents, there were no references to studies done in the Arabian Gulf, and all included studies were from the Western world except for 1 study done in the Middle East (Israel) (Griffiths et al., 2010, Ul-Haq et al., 2012). It has been suggested that the impact of child or adolescent obesity on HRQL is influenced by culture (Hamzaid et al., 2011), but since the evidence base on impairment of HRQL in adolescents is still very limited in geographical scope the hypothesis that culture influences the obesity associated impairment of child or adolescent HRQL has not been tested. For example, it is not clear whether obesity impairs the HRQL of adolescents in the Arabian Gulf States. Deficits in HRQL may drive healthcare utilization by creating a demand for obesity treatment (Hughes et al., 2007, Williams et al., 2005, Schwimmer et al., 2003) and understanding the extent of these deficits in non-western societies is important. Thus, the conclusions from the literature on obesity effects on HRQL in children and adolescents to date cannot necessarily be generalized across the world due to the possibility that differences in culture, demography, economy, education and social characteristics might

alter any effect which obesity might have on quality of life. Nonetheless, research in this area to date so far has showed strong evidence that obesity carries detrimental effects on paediatric HRQL including the physical, social and emotional domains of HRQL (Riazi et al., 2010, Hughes et al., 2007, Pinhas-Hamiel et al., 2006, Williams et al., 2005, Schwimmer et al., 2003, Friedlander et al., 2003, Must and Strauss, 1999, Braet et al., 1997a). Different tools have been used to assess the impact of obesity on HRQL, the main one of which is the Pediatric Quality of Life Inventory version 4.0 (PedsQL™ 4.0). The PedsQL™ comprises of parallel scores of child self-report and parent-proxy report, which is a very useful tool to assess the burden of obesity on the whole family, and the potentially different perspectives of parents and adolescents (Eiser and Morse, 2001) .

So, in order to fill the research gap on the impact of obesity on adolescent HRQL from Gulf States and Non Western countries, we conducted this study on a community sample of obese Kuwaiti adolescents. The primary purpose of this study was to evaluate the association between HRQL and obesity in Kuwaiti adolescents aged 10 to 14 years. The hypothesis is that with increased body mass index centile (BMI), HRQL would be decreased. Information on the HRQL in this age group, who may be at risk of functional limitations and life dissatisfaction, may direct behavioural interventions for improving the care of obese children and adolescents. We carried out a formal paired comparison of HRQL between obese and healthy weight control adolescents to see if there would be any differences. We also wanted to compare the HRQL self-report of adolescents and their parent-proxy reports. To our knowledge, this is the first study to evaluate the relationship between HRQL and obesity in a paediatric sample in Kuwait and the Arabian Gulf region.

4.2 Literature review on HRQL and paediatric obesity

Health related quality of life is the individual's ability to function in relation to his/her current state of health. This ability includes physical, mental and social well-being (Tsiros et al., 2009). The relationship between HRQL and paediatric obesity has been studied by Ul-Haq and colleagues (2012) in their meta-analysis of the association between body mass index and health-related quality of life among children and adolescents, assessed using the Pediatric Quality of Life Inventory Index (PedsQL™ 4.0) (Ul-Haq et al., 2012): the pooled studies came from North America, Europe, Australia and Israel. All studies measured the effect of paediatric obesity on the total, psychosocial and physical domains. Pooled analysis showed a dose-response type relationship between BMI and the total, psychosocial and physical HRQL scores. Obese children and adolescents (ages between 2

and 18 years old) had significantly lower total scores HRQL than normal weight and overweight peers. The psychosocial and physical domains of the PedsQL™ 4.0 questionnaire also differed, however the differences in these domains were not statistically significant. All of these results considered by Ul Haq et al (Ul-Haq et al., 2012) were measured using the self-report forms.

Paediatric obesity remains one of the most common chronic disorders in this age group. The health risks associated with obesity go beyond the physical form to involve almost always psychological aspects (Griffiths et al., 2010, Must and Strauss, 1999, Braet et al., 1997a). Numerous researchers have investigated the medical sequelae of paediatric obesity thoroughly (Weiss and Kaufman, 2008) and there is long history of research conducted to find out the impact obesity has on paediatric physical, functional, emotional and social well-being (Braet and Mervielde 1997(Braet et al., 1997a). This is as important an issue as exploring the physical-medical complications associated with paediatric obesity.
Altogether the physical and mental complications are fundamental in forming the shape of treatment guidelines indicating the need for supportive interventions, prognostic indicators, aid decision making and informing resources allocation and healthcare policy.
Much of a child's or adolescent's life centres around activities with peers and physical performance. In adolescence, transition into school structure and peer network dynamics can provoke distress even in the absence of negative social experiences (Adolescent health, understanding and preventing risk behaviour, 2009). For obese children and adolescents, psychosocial development is usually impaired to a varying extent ranging from weight status and shape dissatisfaction to depression and other psychosocial disorders (Griffiths et al., 2010). The short term psychosocial effects of obesity on children and adolescents include social isolation, discrimination and victimisation by peers. In adolescence, if obesity persists, which is mostly the case (Kuhl et al., 2012, Guo et al., 1994) it can result in negative self-image, and lower self-esteem associated with sadness, loneliness, anxiety and high risk behaviour (Pinhas-Hamiel et al., 2006). In the recent systematic review on self-esteem and quality of life in obese children and adolescents(Griffiths et al., 2010), Griffiths and colleagues showed that the majority of studies conducted using multi-component assessment, including physical, emotional, social and school performance, had strong evidence on an inverse relationship between self-esteem and obesity in that age group, where obesity had its greatest impact on the physical appearance, athletic performance and social wellbeing. However, the Griffiths et al. (2010) evidence base was limited in the number of studies identified (six studies were done on children, 4 studies

done on adolescents, and 5 done on children and adolescents, and all from the Western World). The Griffiths et al. review found that there was no clear evidence as to whether low HRQL in obesity differed between sexes or between different ethnic groups.

One of the main early studies on impairment of HRQL by obesity in children and adolescents was that by Schwimmer et al. (Schwimmer et al., 2003) on a sample of 106 American children and adolescents aged 5 to 18 years old (57 males). Using the PedsQL™4.0 inventory scale, Schwimmer and colleagues found that severely obese children and adolescents had significantly lower HRQL scores in all domains and they were comparable to scores of children and adolescents with cancer.

Williams et al. in Australia (Williams et al., 2005), also used the PedsQL™4.0 index on a community sample of 1456 children and adolescents aged 9 to 12 years old who were categorised into three groups; not overweight (n=1099), overweight (n=294) and obese (n=63). They demonstrated that HRQL scores decreased dramatically in the obese children and adolescents, compared to the overweight and not overweight groups. From Israel, Pinhas-Hamiel et al. (Pinhas-Hamiel et al., 2006) compared results of PedsQL™ 4.0 scores from a community sample and hospital sample of 88 obese adolescents (aged 11-14years) and found no significant difference in HRQL scores between treatment-seeking sample and community sample, however both groups had significantly lower HRQL scores than healthy weight group (n=93), especially in the physical, social and school performance domains. These results only highlight the importance of measuring HRQL in obese paediatric population, regardless of their treatment seeking status (Tsiros et al., 2009).
From the UK, Riazi et al (Riazi et al., 2010) used the PedsQL™ 4.0 inventory scale to compare the HRQL of a clinical sample of 96 obese children and adolescents aged 5 to 16 years old with 444 healthy weight controls with similar age range. Results showed that the obese group had significantly lower scores in all domains than the healthy weight controls (P <0.005).

Some paediatric obesity HQRL studies using the PedsQL™4.0 have investigated the difference between child-self report and parent-proxy report scores. In summary, parent-proxy reports of HRQL tend to be similar to that of child-self reports in that both scores tend to be low in obesity compared to healthy weight controls, but with a larger deficit in the obese when studied by self-report (Kuhl et al., 2012, van Grieken et al., 2012, Varni et

al., 2007, Hughes et al., 2007, Pinhas-Hamiel et al., 2006, Williams et al., 2005, Schwimmer et al., 2003, Wake et al., 2002, Stradmeijer et al., 2000).

Here, effects of obesity on HRQL might possibly be culture-specific. Hughes et al. (Hughes et al., 2007) used the PedsQL™4.0 index to compare child-self report with parent-proxy report of a sample of 126 obese 5 to 11 years old children and adolescents from Scotland. Parents reported lower scores of all domains of the PedsQL™4.0 than self-reports and the difference in score was significantly low for the emotional and social domains. In contrast, Hamzaid et al. (Hamzaid et al., 2011), in 5 to 11 year old obese children and adolescents (n=90) in Malaysia using the PedsQL™4.0 index, observed no significant impairment of HRQL when using parent-proxy reports.

This difference in child's and parent's perspectives highlights the importance of seeking HRQL score of proxy (parent) raters as well as self-reports to gain access to the amount of distress that faces the family as a whole with regards to their child's obesity (Varni et al., 2004). In clinical settings, although it is usually assumed that caregivers can provide more accurate information about the impact the disease has on the child, it is equally important and valid to look into the child's perspective (Eiser and Morse, 2001). And in a research setting, caution should be practiced when utilizing HRQL data from only parent-proxy reports or only from child self-report (Ul-Haq et al., 2012, Tsiros et al., 2009).

Box 2. Main findings from the literature reviews on the relationship between HRQL and obesity

- Obesity has a significant negative effect on total score of Peds QL 4.0 in obese children and adolescents
- Obesity has an inverse relationship with self-esteem in obese children and adolescents
- HRQL measured using Peds QL 4.0 was significantly impaired in severe childhood and adolescent obesity comparable to scores of children and adolescents with cancer
- Parent-proxy reports of HRQL of their obese children is culture-specific
- Most of the research on the relationship between obesity and HRQL comes from the western world and more research is needed from other parts of the world to identify the type of relationship between paediatric obesity and HRQL

4.3 Other psychological complications of paediatric obesity

Depression is another form of psychosocial impairment in obese adolescents. There is evidence showing that both conditions, i.e. depression and obesity, have a cause and effect relationship with each other in that age group (Griffiths et al., 2010, Tsiros et al., 2009).

Several studies showed that acquiring depression in adolescence increases the chance of obesity even after controlling for confounding factors, especially among girls (Richardson et al., 2003, Goodman and Whitaker, 2002).

In social self-perception; the judgment we think others hold on us in relation to our appearance or attitude, age plays an important role in the effect of obesity (Strauss and Pollack, 2003, Phillips and Hill, 1998). In pre-adolescence, social networking and preferences were similar between the obese and the healthy weight, regardless of gender (Phillips and Hill, 1998). In 2003, Strauss and Pollack analysed the data of 90,118 students from the National Longitudinal Survey of Adolescents health (Richardson et al., 2003) on social network mapping and found out that obese adolescents were significantly less likely to be chosen as friends than their normal weight peers. This degree of social rejection can expand to reach the form of victimisation, where obese children and adolescents are more likely to be teased and bullied than their healthy weight peers, and end up with low self-esteem, dissatisfaction with their physical appearance and athletic performance, and possibly eating disorders (Neumark-Sztainer et al., 2002, Kraig and Keel, 2001). Correspondingly, greater school connectedness has been associated with better academic performance and outcome, and lower levels of involvement in health-risk behaviours (Allen et al., 2004)

4.4 Research objectives

The primary aim of this research was to investigate the HRQL of obese Kuwaiti adolescents using PedsQL™4.0 and compare the results with that of HRQL of healthy weight adolescents in order to determine whether the obesity associated impairment of HRQL described in the literature was present in adolescents in Kuwait. Secondly, we wanted to examine differences of HRQL scores between adolescent-self report and parent-proxy report in the obese group, and also test for gender differences in the effect of obesity on HRQL of obese Kuwaiti adolescents. This study, which used the PedsQL™4.0 as its measurement tool, was the first of its kind to be conducted in Kuwait and the Arabian Gulf region. It would test whether the HRQL of obese Kuwaiti adolescents was impaired in relation to the HRQL of matched healthy weight peers.

4.5 Methods

4.5.1 Measurement of HRQL

Health-related quality of life measures are now frequently needed in clinical trials as measures of outcome (Goss and Quittner, 2007). They are subjective measures of one's physical, mental and social well-being in relation to their current state of health. Except in very young children or when children are unwell, these measurement tools can be assessed by children as young as 5 years of age, otherwise, parent-proxy reports are also available (Palermo et al., 2008). Dual reporting where both parents and their children report their perceptions is also used to provide an insight into the whole context of family functioning. Palermo and Colleagues (Palermo et al., 2008) carried out evidence-based review of tools that provide options for either parent or paediatric reports of health-related quality of life. There are two types of HRQL measurements; generic and condition-specific instruments. The generic or non-categorical type, although less sensitive than the condition-specific type, allows for comparison of HRQL of different conditions in a large scale (Palermo et al., 2008). The Paediatric Quality of Life Inventory (PedsQL ™ 4.0, MAPI Research Institute, Lyon, France) is a generic HRQL questionnaire that also has an age-appropriate version and parent-proxy reports (Varni et al., 2001)(See fig 5.1). Using the PedsQL ™ 4.0 questionnaire, Varni and colleagues found that, obese young patients had lower subjective score for their HRQL than patients with cardiac, gastrointestinal, and diabetic conditions. This questionnaire is a well-established, valid and reliable tool that can distinguish between healthy children and children with acute or chronic conditions and is responsive to clinical change over time. It is a multidimensional construct that includes 23 items making the physical, emotional, social and school performance domains from which total, psychosocial and physical scale scores are derived. The physical functioning domain has 8 measurement items, the mean of which makes the physical scale score. The emotional functioning domain has 5 measurement items, the social functioning domain has 5 measurement items and the school functioning domain has 5 measurement items (Varni et al., 2001). The total score can be derived from the mean of all 23 items. The psychosocial scale score can be derived from the mean of items in the emotional, social and school performance domains. Three versions of the subjective report scale are available; the young children report (age 5 to 7 years) where it has a three-point response scale (0 = not at all a problem, 2 = sometimes and 4 = a lot, with each response choice anchored to either smiling, middle or frowning face respectively), the children report (age 8 to 12 years) and the teenagers report (age 13 to 18 years) where the scale has a five-point response (0 = never a problem, 1 = almost never, 2 = sometimes, 3 = often and 4 = almost always). Items

are linearly transformed to a 0 to 100 scale, so that the higher the score, the better the HRQL. The PedsQL ™ 4.0 inventory is available in English, Arabic and many other languages.

4.5.2 Study participants

The present study sample was recruited from public schools in Kuwait city, the Capital of Kuwait. Figure 5.2 outlines the study flow diagram. The Ministry of Education granted us the ethical approval to commence the study in intermediate schools in the Capital in order to cover the age range selected (10 to 14 years). Gathered from the Ministry of Education's archives, the Capital contains a total of 41 males' public intermediate schools and 39 females' public intermediate schools.

Phone calls were made to the management of each of these schools to explain the nature of the study in order to gain access and recruit the study sample. Only 10 of the public intermediate schools gave us appointments and were visited; 3 girls' schools and 7 boys' schools. Permission was granted by the school principals of only three schools; two male and one female school. Screening for height and weight was carried out by two, trained dietetic assistants from the Food and Nutrition Administration department of the Ministry of Health. Grades from five to nine were selected to cover the age range targeted i.e. 10 to 14 years. Screening was carried out on a total of 1042 students. After screening, the researcher collected the height and weight figures of all pupils, calculated the BMI, and plotted the results on the age and gender specific percentile charts. Pupils were categorised into healthy weight group, overweight group and obese group according to reference data from the US Center for Disease Control (CDC) 2000. Obesity was defined as BMI of $\geq 95^{th}$ centile, overweight was defined as BMI $\geq 85^{th}$ centile and $<95^{th}$ centile, and healthy weight was defined as BMI $\geq 3^{rd}$ centile and $<85^{th}$ centile, using gender specific, BMI for age percentile charts. National (Kuwaiti) reference data for BMI to define weight status in that age group was not used. El Ghaziri et al. (2011) proved that using Kuwaiti reference data to define weight status in 10 to 14 years old adolescents underestimated the prevalence of overweight and had the lowest agreement with known international methods namely; Cole-IOTF, CDC 2000, and WHO 2007 (El-Ghaziri et al., 2011).

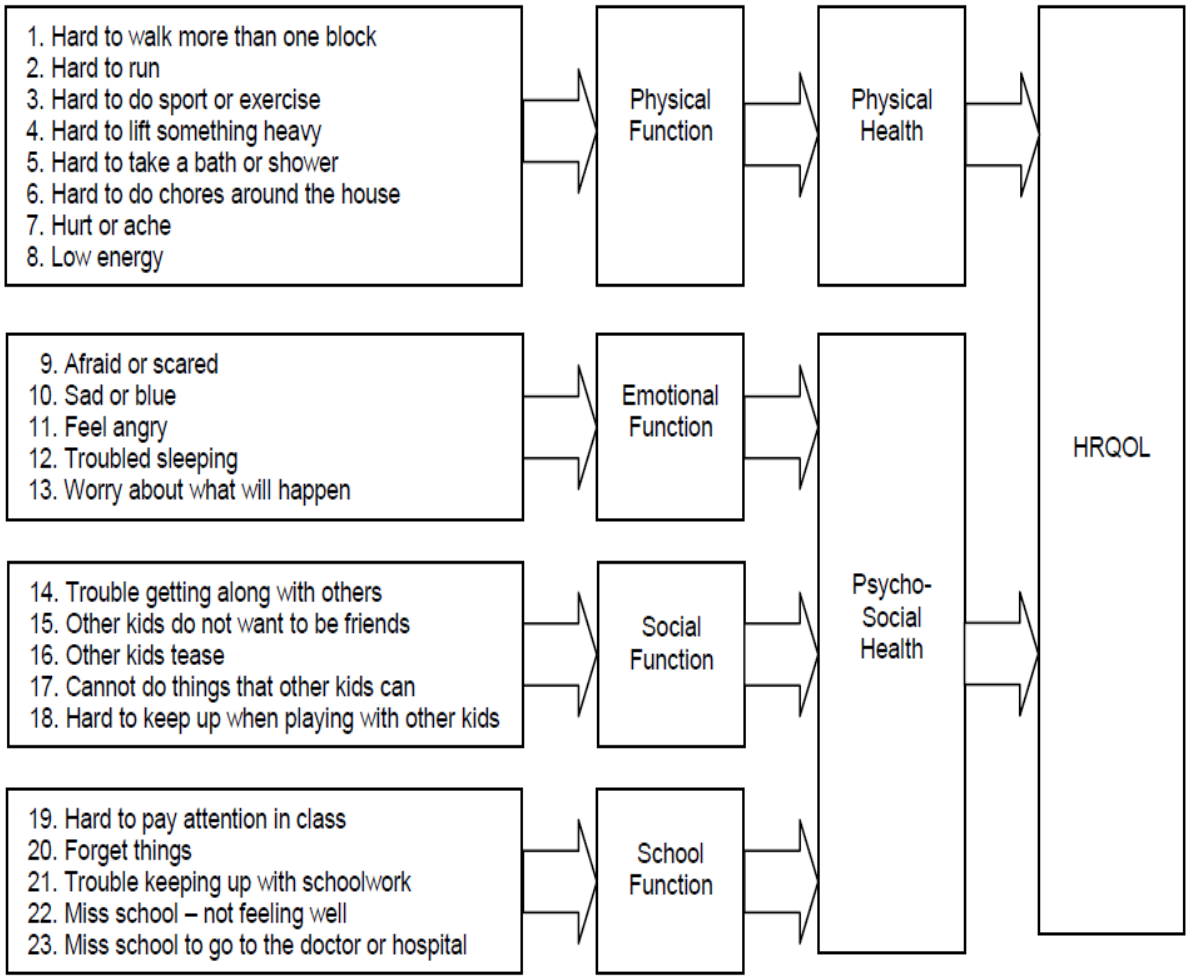

Figure 4. 1 Structure of the multidimentional Peds QL 4.0 generic score scale measuring HRQL in adolescents, adopted from Petersen et al., 2009

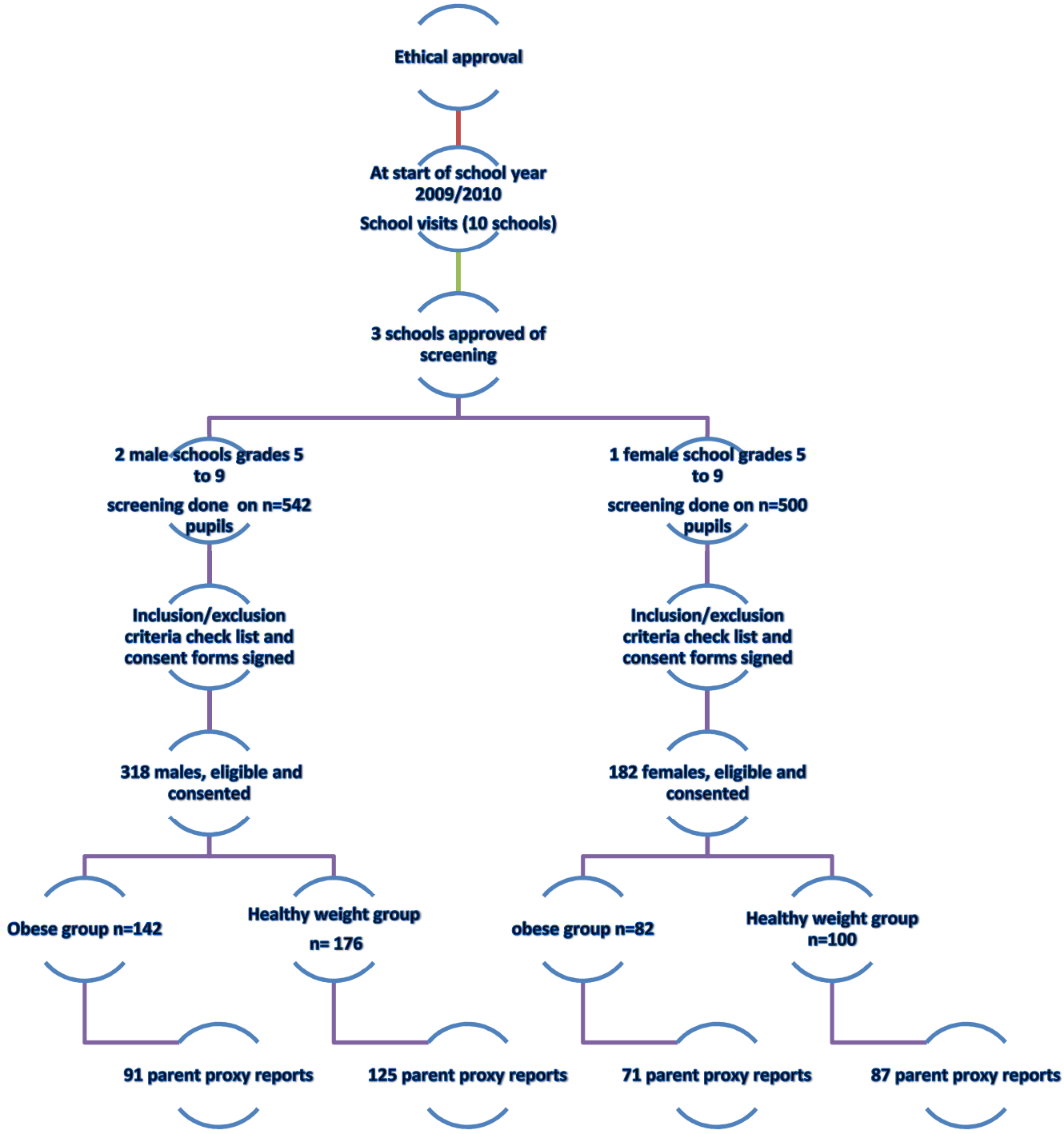

Figure 4.2 Study flow diagram

Only those who were either in the healthy weight or obese categories were selected for the study. Verbal check list of the inclusion and exclusion criteria was presented to each class before giving out the consent and PedsQL™ 4.0 forms to the selected study sample. Participants and their families provided informed written consent. The PedsQL™4.0 Arabic version was completed independently by adolescents at school and their relative parents at home. The study was approved by the Medical Research Committee of the Ministry of Health and the Ethical Committee of the Ministry of Education in Kuwait. A formal matched pairs were formed between the obese group and the healthy weight group according to age and gender. This yielded 98 pairs with 57 paired boys and 41 paired girls, with median age of 12.4 years. There were twelve parents' reports missing. The researcher had to pursue the parents, and filled out the Peds™4.0 forms through phone call interviews; at the end, these reports were included in the final analysis.

4.5.3 Inclusion and exclusion criteria

Subjects were included if they fit the eligible age range (10 to 14 years), were either obese, as defined by the US CDC 2000 definition of BMI $\geq 95^{th}$ percentile, or of healthy weight, defined as BMI $< 85^{th}$ and $\geq 3^{rd}$ percentile. Overweight pupils were excluded from the study sample in order to provide a clear contrast in weight status between the two groups of interest. Exclusion criteria were as follows: the presence of any chronic disease such as diabetes, cardiovascular disease or others; obesity as a result of a known underlying organic cause; the presence of a genetic syndrome; untreated hypothyroidism; and the use of medication that might interfere with the weight of the subject. The total number of pupils who did not fulfill the inclusion criteria was 542, 224 males and 318 females.

4.5.4 Anthropometry

Subjects were measured in light clothing and without shoes. Height was measured to the nearest 0.1 cm using portable
stadiometer (Leicester Height Measure, Child Growth Foundation, Leicester, London, UK). Weight was measured to the nearest 0.1 kg using scales (Tanita™). BMI was calculated as the weight (kg) divided by the height (m^2).

4.5.5 Measurement of the HRQL

The total HRQL score was derived from the mean of all 23 items of the inventory index which included the physical functioning domain (8 items), emotional functioning domain (5 items), social functioning domain (5 items) and school functioning domain (5 items). As

is common in the literature (Varni et al., 2001) psychosocial score was derived from the mean of items in the emotional, social, and school functioning domains (See Fig 1.). The Physical Score is a separate domain (See Fig.1). The analysis was based on the total, psychosocial and physical scores of the obese group, healthy weight group, and parent-proxy reports. All calculations were done manually by the researcher. All HRQL domains were uploaded into excel worksheets, unique for each study group.

4.5.6 Statistical analysis

Data from obese adolescents were not available, and data from Kuwaiti or other Gulf state samples were not available upon which to base a power calculation. In the absence of highly relevant local data the present study power was based on data from a previous power calculation in a comparison of HRQL in obese and non-obese children in Scotland (Hughes et al., 2007). Data from Hughes et al suggested that the sample size required to identify a significant difference between the obese group and the healthy weight group (within each sex, treating boys and girls separately) was a minimum of around 40-43 pairs with 90% power and $p = 0.05$. All the statistical analyses were performed using Minitab 16.0. Data were checked for normality by descriptive statistics and histograms with normal distribution curves. All scores of the PedsQL™4.0 domains were not normally distributed. Matched pairs of obese and healthy weight subjects were selected according to age (age within 10 to 14 years) and gender. Wilcoxon signed-rank tests were used to detect differences in the scores between the obese and the healthy weight groups. We also used Wilcoxon signed-rank test to detect the significance of any difference in scores between self-report and parent-proxy report in the obese group. Regression analysis of predictors of HRQL was also included.

4.6 Results

4.6.1 Sample characteristics

The final study sample consisted of 500 adolescents, all Kuwaiti nationals, 318 boys (63.6%) and 182 girls (36.4%) between 10-14 years of age (median age 12.3). From the study sample, only 374 parent-proxy reports came back (162 or 43% from the obese group and 212 or 57% from the healthy weight group). Data were collected from 224 obese adolescents, and 276 healthy weight adolescents.

The ethnic distribution of the whole sample was similar as all participants were Kuwaiti Nationals. Formal socioeconomic status definition does not exist (Channanath et al., 2013).

Table 4.1 summarises the physical characteristics of the study sample. The normal weight group had 176 males of which only 125 parents provided their parent-proxy reports. Also included in the group 100 female students of which only 87 parents provided their parent-proxy reports. On the other hand, the obese group had 142 obese male students and 82 obese female students of which 91 and 71 parents provided their parent-proxy reports, respectively. The median age for the obese group was 12.4 years (IQR 10.4, 14.0) and median age for the healthy weight group was 12.3 (IQR 10.1, 14.0).

Table 4.1 General characteristics of the obese and healthy weight groups

	Healthy weight group			Obese group		
Variable	n	Median	IQR	n	Median	IQR
Age (years)	276	12.3	(10.1, 14.0)	224	12.4	(10.4, 14.0)
Males	176	12.3	(10.1, 14.0)	142	12.6	(10.8, 14.0)
Females	100	12.2	(10.0, 14.0)	82	12.4	(10.3, 14.0)
BMI	276	18.1	(15.0, 21.1)	224	28.8	(23.3, 34.3)
BMI Z score	276	0.1	(-0.6, 0.5)	224	2.1	(1.9, 2.3)

BMI; body mass index

4.6.2 HRQL of the obese adolescents

4.6.2.1 Total Score

The HRQL data are shown in table 4.2. The total score for the obese self-report ranged from 14.1 to 100.0. The median of the total score for the whole sample (n=224) was 84.8 (IQR 74.2, 95.4). The median of the total score for the obese boys (n=142) was 88.0 (IQR 78.3, 96.7). The median score for the obese girls (n=82) was 79.3 (IQR 70.4, 91.6). In comparison, the total score for the parent-proxy report of the total sample (n=162) ranged from 43.8 to 100.0, with a median score of 78.3 (IQR 62.8, 88.0). Median total score for parent-proxy reports of the obese boys group (n=91) was 76.1 (IQR 65.2, 86.9) and for the obese girls group (n=71) was 81.5 (IQR 60.9, 90.2).

4.6.2.2 Psychosocial Score

The psychosocial score of the obese sample ranged from11.7 to 100.0. The median was 85.0 (IQR 75.0, 93.3), median for the obese boys 87.5 (IQR 78.3, 96.7), and for the obese girls was 82.5 (IQR 70.0, 91.6). The psychosocial score for the parent-proxy report ranged from 30.0 to 100.0. The median score for the obese group 76.7 (IQR 63.3, 88.3), for the obese boys was 87.5 (IQR 78.3, 96.7), and for the obese girls 82.5 (IQR 70.0, 91.6).

4.6.2.3 Physical Score

The physical score of the obese sample ranged from 18.8 to 100.0. The median score for the whole sample was 87.5 (IQR 75.0, 100.0), for the obese boys 90.6 (IQR 78.1, 100.0), for the obese girls 81.3 (IQR 68.0, 96.9).

The physical score for the parent-proxy report ranged from 6.3 to 100.0. The median for the total sample was 82.9 (IQR 59.4, 93.8), for the obese boys 84.4(IQR 62.5, 93.8), and the obese girls 81.3 (IQR 50.0, 93.8).

4.6.3 HRQL of healthy weight adolescents

4.6.3.1 Total Score

Here, the self-report and parent-proxy scores for the total, psychosocial and physical scores are summarised in table 4.3. The sample included 276 healthy weight adolescents, of which there were 176 healthy weight boys and 100 healthy weight girls. A total of 212 parent-proxy reports were obtained, of which 125 from healthy weight adolescents' boys' parents reports and 87 from healthy weight adolescents' girls' parents reports. The total score of the healthy weight adolescents self-reports ranged from 18.5 to 100.0, median was 89.1 (IQR 76.4, 96.7), 92.4 (IQR 78.3, 97.8) for the boys, and 86.4 (IQR 75.0, 95.6) for the girls. Median score for the parent-proxy report was 79.3 (IQR 62.0, 91.3), for the healthy weight boys' parent-proxy reports 82.6 (IQR 69.1, 91.3), and girls' parent-proxy reports 69.6 (IQR 55.4, 87.0).

4.6.3.2 Psychosocial Score

The psychosocial score for the healthy weight controls ranged from 6.7 to 100.0, median was 88.3 (IQR 76.7, 96.7), median for the boys 90.0 (IQR 76.7, 98.3), and for the girls 86.7 (IQR 73.3, 96.7). In comparison, the psychosocial score for the healthy weight parent-proxy report of the whole sample ranged from 20.0 to 100.0, median for the parent-proxy report 76.7 (IQR 63.3, 90.0), for the boys' 78.3 (IQR 66.7, 91.7) and for the girls' 70.0 (IQR 58.3, 86.7).

Table 4.2 Health-related quality of life scores, median (IQR) from self-report and parent-proxy report of the obese group

Variable	Boys	Girls	Total
Self-report	n=142	n=82	n=224
Physical score	90.6 (78.1, 100.0)	81.3 (68.0, 96.9)	87.5 (75.0, 100.0)
Psychosocial score	87.5 (78.3, 96.7)	82.5 (70.0, 91.6)	85.0 (75.0, 93.3)
Total score	88.0 (78.3, 96.7)	79.3 (70.4, 91.6)	84.8 (74.2, 95.4)
Parent-proxy report	n=91	n=71	n=162
Physical score	84.4 (62.5, 93.8)	81.3 (50.0, 93.8)	82.9 (59.4, 93.8)
Psychosocial score	76.7 (66.7, 86.7)	80.0 (61.7, 91.6)	76.7 (63.3, 88.3)
Total score	76.1 (65.2, 86.9)	81.5 (60.9, 90.2)	78.3 (62.8, 88.0)

4.6.3.3 Physical Score

The physical score of the healthy weight group self-reports ranged from 18.8 to 100.0. Median score for the total healthy weight sample was 93.7 (IQR 81.2, 100.0), for boys 96.9 (IQR 84.4, 100.0), and for girls was 87.5 (IQR 77.2, 96.9).

The physical score for the parent-proxy reports ranged from 6.3 to 100.0, median 87.5 (IQR 62.5, 96.9), for the boys' 90.6 (IQR 71.9, 96.9) and for the girls' 75.0 (IQR 50.0, 93.7).

4.6.4 Matched paired comparison of HRQL between the obese vs healthy weight (control) group (n=98 matched pairs)

4.6.4.1 Self-Reports

Formal matched pairs were formed between obese and normal weight groups based on age and gender as shown in table 4.4. There were no statistically significant differences in HRQL between the obese and normal weight adolescents self-reports, using the total score and psychosocial score scales. The median of the total score of the obese group was 84.8 and for the healthy weight group was 88.0 (95% CI -0.5, 7.1; *p* 0.08). The median of the psychosocial subscale for the obese group was 85.0 and for the healthy weight group was 88.3 (95% CI -1.6, 7.5; *p* 0.2). However, the difference in the physical score between the obese group and the healthy weight group was statistically significant with median score for the obese group at 87.5 and median score for the healthy weight group at 90.6 (95% CI 1.5, 9.4; *p* 0.01).

Table 4.3 Health-related quality of life scores, median (IQR) from self-report and parent-proxy report of the healthy weight group

Variable	Boys	Girls	Total
Child self-report	n=176	n=100	n=276
Physical score	96.9 (84.4, 100.0)	87.5 (77.2, 96.9)	93.7 (81.2, 100.0)
Psychosocial score	90.0 (76.7, 98.3)	86.7 (73.3, 96.7)	88.3 (76.7, 96.7)
Total score	92.4 (78.3, 97.8)	86.4 (75.0, 95.6)	89.1 (76.4, 96.7)
Parent-proxy report	n=125	n=87	n=212
Physical score	90.6 (71.9, 96.9)	75.0 (50.0, 93.7)	87.5 (62.5, 96.9)
Psychosocial score	78.3 (66.7, 91.7)	70.0 (58.3, 86.7)	76.7 (63.3, 90.0)
Total score	82.6 (69.1, 91.3)	69.6 (55.4, 87.0)	79.3 (62.0, 91.3)

Table 4.4 Paired comparisons of health related quality of life (HRQL) for the healthy-weight group vs obese group, median (IQR)

	Healthy-weight group	Obese group	95% CI	*p-value*
Variable	n=98	n=98		
Self-report	Median (IQR)	Median (IQR)		
Physical score	90.6 (81.3, 100.0)	87.5 (68.8, 100.0)	1.5, 9.4	0.01
Psychosocial score	88.3 (76.7, 95.0)	85.0 (73.3, 93.7)	-1.6, 7.5	0.2
Total score	88.0 (78.0, 95.7)	84.8 (70.7, 95.7)	-0.5, 7.1	0.08
Parent-proxy report				
Physical score	86.0 (56.3, 96.9)	81.3 (62.5, 93.8)	-4.7, 6.3	0.7
Psychosocial score	76.7 (65.0, 90.0)	76.7 (61.7, 90.0)	-3.4, 5.8	0.7
Total score	79.3 (59.8, 91.3)	78.8 (63.6, 88.0)	-2.8, 6.0	0.5

Healthy-weight and obese group median age 12.4 (2.1); median BMI Z score for the healthy-weight group 0.1 (1.1);

median BMI Z score for the obese group 2.1 (0.4). All pairs were taken from the same school year

4.6.4.2 Parent-proxy reports

As shown in table 4.4 there were no statistically significant differences in parent-proxy reports between the obese group and healthy weight group. In total score, the median for the obese group was 81.3 and for the healthy weight group was 86.0 (95% CI -2.8, 6.0; *p* 0.5). The median of the psychosocial score in the obese group was 76.7 and for the healthy weight group was 76.7 (95% CI -3.4, 5.8; *p* 0.7). And the median for the physical score in the obese group was 81.3 versus 86.0 in the healthy weight group (95% CI -4.7, 6.3, *p* 0.7).

4.6.5 Matched paired comparison of HRQL between obese males vs healthy weight males (n=57 matched pairs)

4.6.5.1 Self-reports

Separate analysis was carried out as shown in table 4.5, to compare self-report and parent-proxy reports between the obese males and the healthy weight males. The median of the total score for the healthy weight males self-reports was 88.0, and for the obese males was 89.1 (95% CI -3.3, 5.4, *p* 0.5). For the psychosocial score, the median for the healthy weight males was 88.3 and for the obese males was 88.3 (95% CI -3.4, 5.9, *p* 0.6). Similarly, the difference in the median of the physical score between the healthy weight males and obese males was not statistically significant; median for the healthy weight males was 93.8 and for obese males was 93.8 (95% CI -1.6, 6.3, *p* 0.2).

4.6.5.2 Parent-proxy reports

The median of the total score for the obese group was 76.1, and for the healthy weight group was 84.8 (95% CI 0.0. 10.9, *P* 0.05), the difference of which is statistically significant. The median of the psychosocial score for the obese group was 75.0 and for the healthy weight group was 80.0 (95% CI -1.6, 10.8; *P* 0.14). The median of the physical score for the obese group was 81.2 and for the healthy weight group was 93.7 (95% CI 0.0-11.0; *P* 0.07).

4.6.6 Matched paired comparison of HRQL between obese females vs healthy weight females (n=41 matched pairs)

4.6.6.1 Self-reports

The data of the female matched pairs are presented in table 4.6. The median of the total score for the obese group was 75.0 and for the healthy weight group was 88.0, statistically significant difference (95% CI 0.5, 13.0, *p* 0.04). In the psychosocial score, there was no significant difference between the obese group (median 80.0) and healthy weight group

(median 86.7) where the 95% CI was -0.8, 13.4 and *p* value of 0.09. However, the difference in the physical score between the obese group (median 78.1) and healthy weight group (median 87.5) was statistically significant where the 95% CI was 3.1, 14.1 and *p* value was 0.01.

4.6.6.2 Parent-proxy reports

None of the differences in the scores between obese group and healthy weight groups were statistically significant as shown in table 4.6. In the total score, median for the obese group was 82.6 and for the healthy weight group was 62.0 (95% CI -14.1, 3.2; *p* 0.2). For the psychosocial score, the median of the obese group was 80.0 and for the healthy weight group was 66.7 (95% CI -11.6, 3.4; *p* 0.3). For the physical score, the median for the obese group was 81.3 and for the healthy weight group 62.5 (95% CI -20.4, 3.1; *p* 0.2).

Table 4.5 Paired comparison of health related quality of life (HRQL) for healthy weight boys group vs obese boys group

	Healthy weight boys	Obese boys	95% CI	*p-value*
Variables	n= 57	n= 57		
Child-self report	Median (IQR)	Median (IQR)		
Physical score	93.8 (84.4-100.0)	93.8 (79.7-100.0)	-1.6, 6.3	0.2
Psychosocial score	88.3 (75.0-95.9)	88.3 (77.5-95.0)	-3.4, 5.9	0.6
Total score	88.0 (76.7-96.7)	89.1 (78.8-95.7)	-3.3, 5.4	0.5
Parent-proxy report				
Physical score	93.7 (68.8-98.5)	81.2 (64.1-93.7)	0.0, 11.0	0.07
Psychosocial score	80.0 (66.7-92.5)	75.0 (60.9-88.3)	-1.6, 10.8	0.1
Total score	84.8 (70.7-93.0)	76.1 (64.1-88.0)	0.0, 10.9	0.05

Table 4.6 Paired comparison of health related quality of life (HRQL) for healthy weight girls group vs obese girls group

	Healthy weight girls	Obese girls	95% CI	*p-value*
Variables	n= 41	n= 41		
Self-report	Median (IQR)	Median (IQR)		
Physical score	87.5 (79.7-98.5)	78.1 (65.6-92.2)	3.1, 14.1	0.01
Psychosocial score	86.7 (77.5-95.0)	80.0 (67.5-92.5)	-0.8, 13.4	0.09
Total score	88.0 (78.3-94.1)	75.0 (68.0-95.1)	0.5, 13.0	0.04
Parent-proxy report				
Physical score	62.5 (46.9-90.6)	81.3 (56.3-96.9)	-20.40, 3.1	0.2
Psychosocial score	66.7 (60.9-85.0)	80.0 (61.7-91.7)	-11.6, 3.4	0.3
Total score	62.0 (54.9-85.9)	82.6 (61.9-90.8)	-14.1, 3.2	0.2

4.6.7 Differences between self-reports and parent-proxy reports for the obese adolescents

Table 4.7 summarises the data of the obese adolescent self and parent-proxy reports. The median age of the sample was 12.3 (IQR 11.3 – 13.4, n=162). There were 91 males for the paired comparison (median age 12.4, IQR 11.4 – 13.4) and 71 females for the paired comparison (median age 12.2, IQR 11.1 – 13.2). All the differences in median of the total, psychosocial and physical scores between obese adolescents' self-report and parent-proxy reports were statistically significant ($p < 0.001$). The differences in in median between male-self report and parent-proxy report of the total, psychosocial and physical scores were all statistically significant ($p < 0.001$), so was the difference in the median of the female-self report and parent-proxy report for the physical score (*p 0.03*). However, the difference in the median of the total score and the psychosocial score between the female-self report and parent-proxy report were not statistically significant (*p 0.06, 0.1, respectively*).

Table 4.7 Comparison between HRQL score of self-report and parent-proxy report for the obese group

	Self-report	Parent-proxy report	95% CI	*p*- value
	Median (IQR)	Median (IQR)		
Males (n=91)				
Total score	89.1 (79.3-96.7)	76.1 (65.2, 86.9)	6.5 - 13.6	< 0.001
Psychosocial score	88.3 (78.3-96.7)	76.7 (66.7, 86.7)	6.7 - 14.2	< 0.001
Physical score	90.6 (78.1-100.0)	84.4 (62.5, 93.8)	3.2 - 12.6	< 0.001
Females (n=71)				
Total score	81.5 (70.7-92.4)	81.5 (60.9, 90.2)	-0.1 - 9.8	0.06
Psychosocial score	83.3 (71.7-91.7)	80.0 (61.7, 91.6)	-0.9 - 9.1	0.1
Physical score	84.4 (65.6-96.9)	81.3 (50.0, 93.8)	0.0 - 12.5	0.03
Total (n=162)				
Total score	86.5 (73.9-95.6)	78.3 (62.8, 88.0)	4.9 - 10.9	< 0.001
Psychosocial score	86.7 (75.0-93.7)	76.7 (63.3, 88.3)	4.2 - 10.8	< 0.001
Physical score	87.5 (75.0-100.0)	82.9 (59.4, 93.8)	3.2 - 11.0	< 0.001

4.6.8 Regression analysis of predictors of HRQL

Age, gender and weight status were considered as potential factors which might influence HRQL in the present study and so were included in regression analysis which aimed to determine if any influence of obesity on HRQL was independent of age and sex (summarised in 4.8).

Table 4.8 Regression analysis of predictors of HRQL (*p*)

Variable	Self-report Total score	Parent-report Total score
Age	0.1	< 0.001
Gender	0.02	< 0.001
weight status	0.1	0.6

From adolescent perspective, age and weight status had no significant predictive association with HRQL in the scale chosen for the analysis i.e. the total score (*p* 0.1 for both factors), however, gender showed some association but was statistically insignificant (*p* 0.02).

In the parent-report analysis, age and gender had significant association with HRQL total score, and obesity had no association (*p* 0.6).

4.7 Discussion

Impact of obesity on HRQL- Main findings and study implications

The present study found few significant differences in HRQL domains between obese Kuwaiti adolescents and healthy weight Kuwaiti adolescents when paired comparisons were made between the obese versus healthy weight groups. The only statistically significant difference found in the paired comparisons was in the physical score, though the total score difference approached significance, though the regression analysis did suggest that obesity was not associated with impairment of HRQL, at least in the total score. Differences between the obese and the healthy weight groups in HRQL were generally smaller than might have been expected from the literature on Western samples of obese children and adolescents (discussed in more detail below)

In the present study, gender was an important factor, as obese females' HRQL scores were generally lower than those of obese males, and in the paired comparisons between obese and non-obese groups differences which were significant emerged in the girls which were not present in the boys(Table 4. 4,4.5, and 4.6). In the regression analyses both female sex and obesity tended to predict lower HRQL and so it seems that HRQL was lower in girls than boys in the present study, and was more impaired in the obese girls than in obese boys.

A summary of the main findings of this study is as follows:

A. Formal matched pairs were formed between the obese and healthy weight adolescents on a total of 98 pairs with median age 12.3 years.
B. The difference in physical score between the pairs was statistically significant *p* 0.007.
C. The difference in the total score approached significance due to the effect of the difference in the physical score between groups (*p* 0.08).
D. No differences were found in parent-proxy reports between the obese and healthy weight groups.
E. Obese boys had similar scores in the physical, psychosocial, and total scores to the healthy weight boys (n= 57).
F. Obese girls had statistically significant difference in the total and physical scores and a trend of lower psychological score (*p* 0.04, 0.006 and 0.09, respectively).
G. Differences between parent-proxy reports and obese adolescents' self-report in total, psychosocial and physical scores were statistically significant ($p < 0.001$).

Impact of obesity on HRQL- Comparisons with other studies

For the purpose of this thesis, it is essential to compare studies coming from different parts of the world which investigated the effect of paediatric obesity on HRQL using the PedsQL™4.0 questionnaire with our study. As mentioned in the introduction; research in this area was carried out primarily from the Western world and more recently the Far East and found that obesity had negative impact on paediatric HRQL (Ul-Haq et al., 2012, Griffiths et al., 2010, Hamzaid et al., 2011, Hughes et al., 2007). So in order to appreciate the magnitude of our findings, comparison with other research findings from different parts of the world should be carried out. Hughes et al. (Hughes et al., 2007) compared the HRQL between obese and healthy weight children aged 5 to 11 years in Scotland. Using PedsQL™4.0 self-report questionnaire, Hughes et al. found that HRQL was impaired in obese children compared to healthy weight peers. They also found that this impairment was much more marked when assessed by parents than by child self-report. In contrast, Hamzaid et al. (Hamzaid et al., 2011) in the MASCOT study (Malaysian Childhood

Obesity Treatment Trial); found that impairment of HRQL in obesity was much more marked when using child-self report rather than parent-proxy report. Table 4.9 displays the median and IQR of the physical score, psychosocial score and total score of the present study, SCOTT and MASCOT. The median of obese Kuwaiti adolescent-self report in the physical, psychosocial and total scores were higher than child-self reports in MASCOT and SCOTT.

One previous study of HRQL in adolescents and young adults in Kuwait: Al-Fayez and Ohaeri (Al-Fayez and Ohaeri, 2011) used a different instrument to measure HRQL and included older participants than those recruited to the present study, 14-23 y olds. In the study by Al-Fayez and Ohaeri (Al-Fayez and Ohaeri, 2011) HRQL scores were lower than in samples from western countries, lower in females than males, but the influence of obesity on HRQL was not considered. The reasons why HRQL is lower in girls than boys was not the main focus of the present study, but was consistent with the findings of Al-Fayez and Ohaeri (Al-Fayez and Ohaeri, 2011).

Table 4.9 Health-related quality of life scores, median (IQR) from obese child-self report of Kuwaiti adolescents (10 to 14 years), Malaysian children (9.6 to 10.5 years) and Scottish children (5 to 11 years)

Variable	Child self-report	Parent-proxy report
Kuwait(Boodai and Reilly, 2013)	n=162	n=162
Physical score	87.5 (75.0-100)	82.9 (59.4-93.8)
Psychosocial score	86.7 (75.0-93.7)	76.7 (63.3-88.3)
Total score	86.5 (73.9-95.6)	78.3 (62.8-88.0)
Malaysia (MASCOT)(Hamzaid et al., 2011)	n=90	n=90
Physical score	82.9 (65.7-90.6)	67.2 (59.4-81.3)
Psychosocial score	62.5 (53.3-75.4)	62.5 (53.3-75.4)
Total score	76.1 (64.1-84.8)	65.2 (57.3-76.1)
Scotland (SCOTT)(Hughes et al., 2007)	n=126	n=126
Physical score	75.0 (61.7-84.4)	71.8 (59.4-81.2)
Psychosocial score	73.3 (61.3-83.3)	65.0 (54.8-76.7)
Total score	73.7 (62.4-82.8)	65.6 (56.7-77.8)

Median HRQL scores in the Kuwaiti parent-proxy reports in the present study were higher than that of parent-proxy reports in the studies in Scotland and Malaysia (Hamzaid et al 2011, Hughes et al. 2007). This basic comparison raises the question of whether HRQL of obese Kuwaiti adolescents, while there was evidence that it was impaired in the present study, was impaired to the extent that this was a problem. Another way of looking at it is whether the HRQL scores of the present study samples were at the low end or below the low end of the normal range, but no thresholds or 'normal range' for diagnosis of low HRQL exists at present

Differences between adolescent-self report and parent-proxy report-main findings and study implications

The present study showed that parent-reported HRQL was significantly lower than adolescent-reported HRQL in all measured domains. This discrepancy in scores does not mean exaggerated parents' perception of their child obesity, nor does it suggest the invalidity of the adolescents' perception of their disease. It might simply reflect how parents see their child's obesity problem as having greater implications for their physical functioning and social wellbeing than the adolescents perceive (Eiser and Morse, 2001). Beside the present study, many paediatric obesity studies find that parent-proxy reports of HRQL to be lower than paediatric-self reports (Hughes et al., 2007, Pinhas-Hamiel et al., 2006, Schwimmer et al., 2003). However, other studies have found smaller or no significant differences between parent and child/adolescent self-reports (Hamzaid et al., 2011, Williams et al., 2005). It has been suggested that these differences between paediatric and parent perceptions of the paediatric HRQL in relation to obesity emphasises the importance of using both paediatric-self reports and parent-proxy reports when assessing HRQL of obese children and adolescents (Ingerski et al., 2007). It has also been suggested that these differences could have been the driving force for parents to seek professional help for their children's obesity (Tsiros et al., 2009) and this help should be offered for the whole family, not only the obese child.

4.7.1 Strengths, limitations and future research

The present study is the first to date describing HRQL in a community sample of obese Kuwaiti adolescents. It was done on a 224 obese Kuwaiti adolescents and compared their HRQL score with 276 healthy weight peers, which provided adequate power. The use of a valid and reliable HRQL measurement tool (PedsQL ™ 4.0) on such a large and homogenous sample also adds to the strengths of the present study. However, possible

confounding factors like race and socioeconomic status could not be accounted for in this study. In Kuwait, no official definition of social class is present. Also, no consensus exists within the research community on how to define social class in this state with one of the highest per capita incomes in the world. One other limitation is the possibility of sampling error; it is not clear how representative the sample selected is and a study with a representative sample would have been ideal.

On the other hand, further studies in other samples with other age range and other settings are required in order to reach consensus regarding HRQL and obesity in Kuwaiti paediatric population, so that for example any effects of obesity on HRQL in children (rather than adolescents) can be determined, and also determine any effects of obesity on clinical sample of obese children/adolescents.

4.8 Conclusion

The present study suggests that quality of life might not be impaired very dramatically in a community sample of obese Kuwaiti adolescents. Any obesity-related HRQL impairment may be more marked in girls than boys and may be more marked when parent-proxy reports are used than when self-reports are used. However, it also recommends the need for more educational and informative community programmes to increase population's perception on the impact of obesity on health in general and quality of life in specific. As for treatment objectives, it recommends that intervention programmes for the treatment of adolescents' obesity in Kuwait should be directed at both adolescents and their parents. This resilience in adolescents' HRQL should be considered when constructing treatment protocols.

5. Cardiometabolic Risk Factors in a Sample of Obese Kuwaiti Adolescents

BOODAI, S. A., CHERRY, L., SATTAR, N. & REILLY, J. J. In press-a. Prevalence of cardiometabolic risk factors and metabolic syndrome in obese Kuwaiti adolescents. Diabetes Metab Syndr Obes. Appendix F.

5.1 Introduction

Childhood and adolescent obesity increase the risk of both current and future health disorders as noted in chapter 1 (Reilly, 2006, Dietz, 1998). Childhood and adolescent obesity is associated with insulin resistance, abnormal glucose metabolism, hypertension, dyslipidaemia, inflammation, liver disease and compromised vascular function (Franks et al., 2010, Lenz and Diamond, 2008, Freedman et al., 2001, Kolterman et al., 1981). As with obesity, these impairments could track into young adulthood which increases the risk of cardiometabolic diseases and even certain types of cancer independent of adult weight (Beauloye et al., 2007, Reilly et al., 2003). This is an important public health issue which reflects the need for policy for early detection, timely treatment, and development of prevention and treatment interventions for this specific group.

Therefore, this chapter focuses on the assessment of these cardiometabolic risk factors in a reasonably homogenous sample of obese Kuwaiti adolescents undergoing educational group therapy for the treatment of their obesity (NATTO, as described in chapter 6).

The detrimental effects of adolescent obesity on subsequent risk of cardiovascular disease are partly mediated by the presence of cardiometabolic risk factors (Juonala et al., 2011). Cardiovascular disease is the leading cause of morbidity and mortality worldwide with an estimate of 17.3 million deaths in 2008 and by 2030 this number could reach up to 23.3 million (Alwan, 2011). It is widely believed that atherosclerosis begins in childhood and progresses into adulthood (Strong et al., 1992, Zieske et al., 2002). Results from the Bogalusa Heart Study, a prospective study in the USA following children for cardiovascular risk factors since 1972, showed that as the number of cardiovascular disease risk factors increase in childhood, so does the severity of both coronary and aortic atherosclerosis in young adulthood (Freedman et al., 2001). In the Netherlands, 2/3 of the severely obese children and adolescents had more than one cardiovascular disease risk factor in one study (van Emmerik et al., 2012). In Germany and Switzerland around 50% of obese children have at least one cardiometabolic risk factor (l'Allemand-Jander, 2010).

These cardiometabolic risk factors exert their effects on endothelial function and structure resulting in endothelial dysfunction, carotid intimal thickness and increased arterial stiffness (Beauloye et al., 2007, Skilton and Celermajer, 2006, Balagopal et al., 2005, Iannuzzi et al., 2004). Thus the presence of these cardiometabolic risk factors does not necessarily suggest morbidity at a young age, but can predict the early development of cardiovascular disease which will be manifest later in life.

The presence of obesity in childhood and adolescent is also related to the development of fatty liver or steatosis, which is the most common liver abnormality in this age group (Schwimmer et al., 2006). Steatosis can exist with or without elevated liver enzymes (aminotrasferases) (Strauss et al., 2000). For the long term, the ramifications of having persistently elevated liver enzymes and steatosis are very important and could lead eventually to the development of cirrhosis (Weiss and Kaufman, 2008, Schwimmer et al., 2006).

In the present study we carried out assessments of obesity-related cardiometabolic risk factors that could impair vascular health and liver function. These included lipid profile (Cholesterol, LDL, VLDL, HDL, TG), IL-6, ICAM, CRP, adiponectin, liver function tests (ALT, AST, gGT) and insulin resistance (described in detail in the next section). To date, there are no published studies on the prevalence of these risk factors among Kuwaiti adolescents.

The main original intention of the present study was to measure these cardiometabolic risk factors before and after initiation of a family-based obesity treatment intervention (NATTO, described in chapter 3) and to test whether these risk factors changed during the course of weight management. This plan had a potential value in directing and shaping future treatment interventions done in Kuwait. Finding the prevalence of cardiometabolic risk factors in a sample of obese Kuwaiti adolescents could potentially persuade families to take part in future treatment trials, if they knew that some of these risk factors could be present in their children and pose a threat to their health. Finding that cardiometabolic risk factors change positively during weight management would probably encourage future obesity treatment efforts in Kuwait.

In fact, the assessment of cardiometabolic risk factors in the present study was cut short, and only baseline measures were taken due to difficulties faced with the authorising body

in the Ministry of Health-Kuwait (see discussion). However, having baseline data on cardiometabolic risk factors still provided valuable information on the extent of these risk factors in a group of obese Kuwaiti adolescents, and might be a useful tool to engage families in treatment interventions in future (chapter 6). So in the end the main aim of the present study was to establish the prevalence of novel (adiponectin has not been measured in obese Kuwaiti adolescents before) and traditional cardiometabolic risk factors in obese Kuwaiti adolescents, in order to establish whether such measures might be useful to encourage greater engagement with obesity treatment in future adolescent obesity treatment trials in Kuwait.

5.2 Methods

5.2.1 The cardiometabolic risk factors

5.2.1.1 Dyslipidaemia

Cholesterol, VLDL, LDL, HDL and TG

Cholesterol is a steroid that is synthesised in many types of tissue, but particularly in the liver and the intestinal wall (Harvey and Ferrier, 2011). Approximately three quarters of cholesterol is newly synthesised and a quarter originates from dietary intake. It is a structural component of all cell membranes, modulating their fluidity, and, in specialised tissues, cholesterol is a precursor of bile acids, steroid hormones, and vitamin D (Harvey and Ferrier, 2011).

Very low density lipoproteins (VLDL) are composed mainly of endogenous triacylglycerols (TAG) and are produced in the liver. Their function is to carry TAG from the liver to the peripheral tissue (Harvey and Ferrier, 2011).

Low density lipoproteins (LDL) are derived from VLDL by the action of lipoprotein lipase in the plasma. They are rich in cholesterol and cholesterol esters. The primary function of LDL particles is to provide cholesterol to peripheral cells or return it to the liver (Harvey and Ferrier, 2011).

High density lipoproteins (HDL) are responsible for the reverse transport of cholesterol from the peripheral tissue to the liver (Harvey and Ferrier, 2011). Here, cholesterol is transformed into bile acids ready for excretion into the small intestine via the biliary tract (Harvey and Ferrier, 2011).

Dyslipidaemia occurs when there is impairment in the lipid profile of an individual characterised by the presence of one or more of the following: elevated total cholesterol, elevated LDL, elevated TG, low concentration of HDL. The association between dyslipidaemia and atherosclerosis is well established and is considered the primary risk factor for its development (Herouvi et al., 2013). Atherosclerotic lesions cause structural damage through accumulation of fatty streaks in the arterial wall obstructing the lumen and reducing the blood flow to varying degrees. This can lead to the development of coronary artery disease, stroke, aortic aneurysm, and peripheral vascular disease (Baker et al., 2008, Gielen and Hambrecht, 2004, Strong et al., 1992). However, the diagnosis and treatment of dyslipidaemia can reverse these conditions (Herouvi et al., 2013, Beauloye et al., 2007, Zieske et al., 2002, Strong et al., 1992, Holman et al., 1958).

There has been pathological evidence of atherosclerosis in adolescents and young adults with obesity. According to the Pathobiological Determinants of Atherosclerosis in Youth (PDAY) study (McMahan et al., 2006, McGill et al., 2002), the prevalence of atherosclerotic lesions in coronary arteries of humans aged 15 to 35 is higher in males and increases with BMI and panniculus adiposus thickness (abdominal subcutaneous fat). The typical dyslipidaemic pattern in obese children and adolescents is characterised by elevated total cholesterol, elevated TG, top normal to mildly elevated LDL and decreased HDL, compared to healthy weight controls (Friedland et al., 2002, Kwiterovich, 2008), and this profile could track into adulthood. In fact, results from the Bogalusa Heart Study showed that obese adolescents who continue to be obese adults have a 2.4, 3.0 and 8.0 times higher chance of having abnormal LDL, TG and HDL levels, respectively, than those who were and remained lean (Srinivasan et al., 1996). Juonala and colleagues (Juonala et al., 2011) had collected data from large prospective studies namely the Bogalusa Heart study (USA), the Muscatine study (USA), the Childhood Determinants of Adult Health study (Australia) and the Cardiovascular Risk in Young Finns Study (YFS, Finland) with sample size of 6328 subjects that were followed from childhood for an average of 23 years. Obesity was defined using the International Obesity Task Force definition for children and BMI cutoff of 30 for adults. Obese adults who were obese children, as compared to healthy weight adults who had their weight in the healthy range during childhood, had a 1.8 increased risk of elevated LDL, 2.1 increased risk of decreased HDL level, 3.0 fold increased risk of elevated TG ($p \leq 0.002$ for all comparisons). In a sample of 26,000 6 to 18 year old obese children and adolescents from Germany and Switzerland, 32% had one or more lipid profile abnormality (l'Allemand-Jander, 2010).

5.2.1.2 Inflammatory markers

It is well established that obesity is associated with a state of chronic low grade inflammation (Yudkin et al., 1999, Gustafson et al., 2007), in children and adolescents (Ford et al., 2004, Warnberg et al., 2004, Visser et al., 2001).

Adipose tissue serves as an organ for lipid storage and also plays a major endocrine role in secreting various adipokines like leptin and adiponectin as well as other immune related mediators involved in inflammation. These mediators include pro-inflammatory cytokines such as interleukin-6 (IL-6), which in turn activate the synthesis of hepatic acute phase inflammatory proteins such as C-reactive protein (CRP), and therefore adipose tissue has a key role in the mechanism of low grade chronic inflammatory state associated with obesity (Trayhurn and Wood, 2004).

The pathophysiological process of the development of atherosclerotic lesions involves local inflammation as a promoter of fatty deposits and plaque formation (Lind, 2003). One of these inflammatory promoters is CRP. CRP is a protein synthesised in the liver and plays a major role for complement system activation as part of the body defence mechanism against infections. Elevated CRP level is considered an independent pro-atherogenic factor due to its roles in stimulating endothelial production of adhesion molecules, mediating the attraction of monocytes in the area of the atherosclerotic lesions, mediating the uptake of LDL into macrophages which is novel mechanism for foam cell formation prior to fatty deposition (Jarvisalo et al., 2002). Therefore, CRP measurements are useful for the detection and monitoring of the inflammatory status of the body.

CRP levels have been shown to be higher in obese than in healthy weight adults and children (Trayhurn and Wood, 2004, Jarvisalo et al., 2002, Visser et al., 2001, Yudkin et al., 1999). This may be related to the overexpression of the cytokine interleukin-6 (IL-6) from the excessive adipose tissue and its release to the circulation where it is considered the primary promoter of the synthesis of CRP by the liver (Visser et al., 2001).

IL-6 is a cytokine secreted by activated macrophages and lymphocytes. However, third of the total secreted levels of IL-6 comes from adipose tissue, particularly visceral adipose tissue (Yudkin et al., 2000). There are other cytokines released by adipose tissue such as tumour-necrosis factor α (TNF-α). IL-6 was found to be significantly elevated in obese adolescents compared to healthy weight controls (Makni et al., 2013).

Priming the endothelial cells for the atherosclerotic plaque formation depends on the release of cell adhesion molecules expressed on the surface of endothelial cells. These adhesion molecules facilitate the binding of monocytes and lymphocytes to the endothelium in the early stages of atherosclerosis development. Of these adhesion molecules are the vascular cell adhesion molecule (VCAM) and intracellular adhesion molecule (ICAM). Circulating levels of these adhesion molecules are considered predictors for acute vascular events (Lind, 2003). Obesity in adults (Straczkowski et al., 2002) and children (Martos et al., 2009) has been associated with higher levels of circulating endothelial adhesion molecules such as ICAM. The hypothesis behind this association is related to the release of CRP (see earlier) and of angiotensinogen and angiotensinogen converting enzyme by adipocytes, a system that contribute of the vasoconstriction and also stimulates the production of ICAM from the dysfunctional endothelium (Herouvi et al., 2013, Gustafson et al., 2007).

5.2.1.3 Anti-inflammatory markers in adipose tissue

Adiponectin is an adipokine (a protein synthesised only in adipose tissue) which has an anti-inflammatory action. It inhibits phagocytosis, inhibits TNF-α production by macrophages, plays a key role in modulating insulin sensitivity as well as having anti-atherogenic activity (Trayhurn and Wood, 2004). Its secretion is markedly reduced in obesity, insulin resistance and type 2 diabetes (Gustafson et al., 2007). In obese children and adolescents, adiponectin levels are low and this is associated with elevated inflammatory markers, mainly CRP (Winer et al., 2006). From the Bogalusa Heart Study, in a sample of 835 24 to 42 year old adults, the mean adiponectin levels were lower for every 1 mm of childhood skinfold thickness (Toprak et al., 2011). It has been suggested that adiponectin could be used as a marker for metabolic syndrome in children and adolescents (Winer et al., 2006). Reductions in the BMI of obese children and adolescents could increase adiponectin and HDL levels (Herouvi et al., 2013).

5.2.1.4 The metabolic syndrome (MS)

A clustering of cardiovascular disease risk factors in adults was first described by Reaven in 1988 (Reaven, 1988) and was termed by the Metabolic Syndrome (MS), Syndrome X, or Insulin Resistance Syndrome. It is characterised by the presence of central obesity, hypertension, dyslipidaemia with high TG concentrations and low HDL concentrations, and hyperglycaemia (Sovio et al., 2013, Gustafson et al., 2007). The diagnosis in adults is made when three out of these five criteria is present (Alberti et al., 2009). Such a clinical

profile predisposes the individual to develop atherosclerotic cardiovascular disease (ACVD) and type 2 diabetes mellitus. Mortality from ACVD is nearly doubled in individuals suffering from MS compared to the normal population and these individuals have 3 to 4 times increased risk of developing ACVD (Haffner, 1999).

The definition of MS in children and adolescents is not yet standardised, but the need to identify children and adolescents with increased risk of developing cardiovascular disease and diabetes type 2 remains extremely important (Reinehr et al., 2007). Several studies have found clustering of components of MS in the paediatric population. For example; paediatric obesity and hypertension (Salman et al., 2010, Angelopoulos et al., 2006); paediatric obesity and glucose intolerance or type 2 diabetes (Sinha et al., 2002); paediatric obesity and dyslipidaemia (Korsten-Reck et al., 2008), Paediatric obesity, insulin resistance and dyslipidaemia (Sinaiko et al., 2005). Identifying children and adolescents with components of MS could help prevent future adult risk of cardiovascular disease and diabetes. In a prospective 25 year-long study, the Princeton Lipid Research Clinics Follow-up Study showed that 4% adolescents (n=771, mean age 12. 9 years) had ≥ 3 components of MS, 77% of which were obese, and at follow-up, 27.2% of the 771 cohort had MS as adults (mean age 38 years) 6 of them had CHD (Morrison et al., 2007). Morrison and colleagues recommend early intervention to treat and prevent paediatric obesity to overcome the future clinical complications in adults (Morrison et al., 2007). However, the tracking pattern of MS criteria from childhood to adulthood according to a joint statement from the American Heart Association Atherosclerosis, Hypertension, and Obesity in the Young Committee of the Council on Cardiovascular Disease in the Young; Council on Cardiovascular Nursing; and Council on Nutrition, Physical Activity, and Metabolism is unstable especially among adolescents and they have called for the assessment of cardiometabolic risk factors instead of having to assess the presence of MS especially in the clinical context (Steinberger et al., 2009). Furthermore, the definitions of MS in paediatrics were traditionally either based on adult cut off points or use a single set of cut points for all ages. To resolve this issue, the International Diabetes Federation in 2007 published a set of paediatric MS criteria based on percentile definitions intended to be standard across the age range 6 to 16 (Zimmet et al., 2007). Subsequently, the application of the IDF definition has not been uniform across researchers and thus the prevalence of paediatric MS remains variable as a result of lack of a universal definition and variation in the definition used (Steinberger et al., 2009). Reinehr and colleagues (2007) compared the prevalence of MS among 1205 Caucasian overweight 4 to 16 year old Germans using eight

proposed definitions (Reinehr et al., 2007). The prevalence of MS varied significantly ($p<0.001$) and ranged from 6 to 39% depending on the definition used. These definitions included Weiss et al. (Weiss et al., 2004), Viner et al. (Viner et al., 2005), de Ferranti et al. (de Ferranti et al., 2004), Cook et al. (Cook et al., 2003), the WHO (Alberti and Zimmet, 1998), The National Cholesterol Education Program Adult Treatment Panel (ATP III) (2001), the European Group for the Study of Insulin Resistance (EGIR) (Balkau and Charles, 1999), and the IDF (Zimmet et al., 2007).

5.2.1.5 Insulin resistance

Insulin resistance, both in diabetic and nondiabetic individuals, is often associated with obesity, especially central obesity (Yudkin, 2003). The level of resistance occurs in both liver and skeletal muscles. This obesity-associated insulin resistance has been attributed to the presence of free fatty acids (FFAs), released through lipolysis of TG, which impairs insulin action in both hepatocytes and myocytes. Furthermore, many inflammatory cytokines released from adipocytes, such as TNF-α and IL-6, have inhibitory effect on insulin signalling and glucose uptake (Yudkin, 2003). Insulin resistance leads to a state of hyperinsulinaemia in order to produce a euglycaemic state, exhausting pancreatic β-bells and eventually leading to type 2 diabetes mellitus (Keskin et al., 2005).
Quantifying insulin resistance is of great importance for clinical and epidemiological purposes. Methods of varying degrees of complexity exist for each of these purposes. One simple widely used surrogate index is the homeostatis model assessment (HOMA), which depends on blood insulin and glucose concentrations under fasting conditions using the equation; (fasting glucose x fasting insulin)/22.5 (Muniyappa et al., 2008).

5.2.1.6 Non-alcoholic fatty liver disease (NAFLD)

This is a broad term describing hepatic histological changes ranging from non-specific steatosis or fatty change to non-alcoholic steatohepatitis (NASH) which is a condition of having more than 5% of hepatocytes containing fat, degenerative changes and fibrosis. The diagnosis is made when ultrasound test shows fatty changes in the liver or with histological assessment (Welsh et al., 2013). There is no standard cut off value for serum ALT and AST but the most commonly used cut off point is a serum level of >40 U/L (Sohn et al., 2013, Schwimmer et al., 2005) and >35 U/L for gamma-glutamyl transpeptidase (GGT; a biliary system enzyme) (Strauss et al., 2000).The condition is strongly associated with obesity and insulin resistance and is one of the most common liver disease worldwide (Koebnick et al., 2009, Schwimmer et al., 2008, Younossi et al., 2002) and is the most

common liver disease seen in paediatrics (Koebnick et al., 2009, Schwimmer et al., 2006). In Europe, NAFLD was present in 11 to 29% of overweight and obese children in two large studies, predominantly in boys (Wiegand et al., 2010, Reinehr and Toschke, 2009). Obese children diagnosed with NAFLD might also have cardiovascular disease risk factors including dyslipidaemia and hypertension (Schwimmer et al., 2008). More recently in USA the prevalence of NAFLD affects nearly 11% of the total population of the adolescents, a figure that has doubled over the past 20 years, with significant contribution of obesity as a risk factor (Welsh et al., 2013). However, data demonstrate that not all overweight and obese children and adolescents even with biopsy-proven NAFLD have raised levels of liver enzymes (Fracanzani et al., 2008).

5.2.2 Study participants

Participants in the present study were invited from among participants in the NATTO study (n=82, see chapter 2), a treatment intervention for adolescent obesity in Kuwait described earlier in the thesis (chapter 2). Eighty participants aged 10 to 14 years (40 males) consented and underwent a baseline clinical examination, prior to the start of the NATTO study in 2009 and were diagnosed with obesity (BMI $\geq 95^{th}$ percentile for age and sex according to US CDC reference data). The participants had no other morbidities and were willing to provide blood samples for the current study.

5.2.3 Blood sampling

Data were collected on the 80 obese adolescents (age 10-14 years) who participated in the National Adolescent Treatment Trial for Obesity (NATTO) RCT in 2009. Participants and their parents signed an informed consent form. The study was approved by the Ethics Committee for Medical Research-Ministry of Health-Kuwait.

Participants underwent clinical examination including anthropometric assessment by the author. Blood sample collection was carried out by the author and it took place at 8 am in the outpatient clinic after an overnight fast (8-12 hours). The fasting state was verbally confirmed by the participants before sampling. Venous blood was obtained. Blood samples were collected directly in a 10-ml tubes containing EDTA as an anticoagulant. Blood samples were then immediately placed in ice and centrifuged (GS-6KR, Beckman Instruments, Inc, California, USA) within 15-30 minutes of collection for 15 minutes at 3000 rpm and 4°C. EDTA plasma was pipetted into 5 aliqouts of 0.5 ml Eppendorf tubes (Treff Lab, Switzerland) and frozen immediately at 70°C for subsequent analysis.

5.2.4 Blood sample analysis

Cholesterol, TG, HDL, sensitive CRP, ALT, AST and gGT assays were performed by Dr Lynne Cherry of the Metabolic Medicine Group of the Cardiovascular and Medical Sciences division based at the BHF-GCRC Building at University of Glasgow using a C311 Roche analyser. Sensitive CRP immunotubidimetric assays with cholesterol, TG, HDL, ALT, AST, and GGT being enzymatic colorimetic. Kits were supplied by Roche Diagnostic Gmbh.

VLDL and LDL results were calculated using the Friedwald equation:

LDL (mmol/L) = total cholesterol – (HDL + TG / 2.19)

VLDL (mmol/L) = total cholesterol – LDL – HDL

The manufacturer and supplier of these kits is Roche Diagnostics Gmbh, D-68298 Mannhein, Distribution in USA: Roche Diagnostics Corporation, Indianapolis, IN, USA. IL-6, ICAM, adiponectin and insulin analysis (ELISAS) was carried out by Dr Lynne Cherry of the Metabolic Medicine Group of the Cardiovascular and Medical Sciences division based at the BHF-GCRC Building at University of Glasgow. Kits supplied by R&D Systems Europe Ltd. (19 Barton Lane, Abingdon Science Park, Abingdon, OX 14 3NB, United Kingdom) and Mercodia AB. A Multiskan Ascent Plate reader and Ascent Software were used for calculation of results. Human IL-6 HS, cat nos HS600B. Human adiponectin, cat nos DRP300. Human ICAM, cat nos DCD540. Multiskan Ascent Plate reader and software supplied by Thermolife Sciences, Unit 5, The Ringway centre, Edison Road, Basingstoke, Hampshire, RG21 6YH, United Kingdom. Mercodia Ultrasensitive Insulin ELISA, cat nos 10-1132-01 (Mercodia AB, Sylveniusgatan 8A, SE-754 50 Uppsala, Sweden).

5.2.5 The cut off points and definitions for the cardiometabolic risk factors

Table 5.1 shows the cut off points for the cardiometabolic risk factors measured. The cardiometabolic risk factors included fasting blood glucose (FBG), Fasting insulin, homeostatic model assessment for insulin resistance (HOMA-IR), systolic and diastolic blood pressure, lipid profile (cholesterol, HDL, LDL, and TG), Liver function tests (ALT, AST, GGT), and inflammatory markers (CRP, IL-6, ICAM, and adiponectin).

There are two commonly used cut off points for Fasting blood glucose(FBG, mmol/L), the WHO normal cut off < 6.1 mmol/L (WHO, 2006) and the American Diabetes Association normal cut off < 5.6 mmol/L (Genuth et al., 2003). However, in Kuwait the official criterion used for diagnosing and classifying diabetes mellitus is the WHO criterion (Ahmed et al., 2013) and so that was used in the present study.

The resistance of the body to the action of insulin due to obesity results in overproduction of this hormone by the pancreas. Ideally, hyperinsulinaemia is defined if insulin level exceeds the normal value according to the pubertal stage due to the impact of physiological insulin resistance of puberty (Alberti and Zimmet, 1998). However, Tanner staging was not assessed during the clinical examination in the present study for social and cultural reasons, thus standard values of normal, borderline and high fasting insulin levels proposed by American Heart Association scientific statement was chosen (Williams et al., 2002) (table 5.1).

Table 5.1 Cut off points of blood parameters

	Normal	Borderline high	High	Reference
TC, mmol/L	< 4.40	4.40 - 5.15	≥ 5.18	
LDL, mmol/L	< 2.85	2.85 - 3.34	≥ 3.37	
HDL, mmol/L	> 1.66	1.55-0.91 (Borderline-low)	≥ 0.91 (low)	(NECP Panel, 1992)
TG, mmol/L				
2-9 y	< 0.85	0.85 - 1.12	≥ 1.13	
10-19 y	< 1.02	1.02 - 1.46	≥ 1.47	
FBG, mmol/L	< 6.10	6.10 - 6.90 (IFG)	≥ 7.00 (DM)	(WHO, 2006)
ALT, mmol/L	≤ 40.00		> 40.00	(Siest et al., 1975,
AST, mmol/L	≤ 40.00		> 40.00	Strauss et al., 2000,
GGT, mmol/L	≤ 35.00		> 35.00	Schwimmer et al. 2005)
Fasting insulin, mU/L	< 15.00	15.00 - 20.00	> 20.00	(Williams et al., 2002)
CRP, mg/L	< 1.00	1.00 - 3.00	> 3.00	(Pearson et al., 2003)
IL-6, pg/ml	1.00 - 3.90		> 3.90	(Makni et al., 2013)
ICAM, ng/ml				
6-10 y	206.80 - 486.80		> 486.80	(Andrys et al. 2000)
11-15 y	184.10 - 354.00		> 354.00	
Adiponectin, µg/ml	> 10.00		< 5.00 (low)	(Goksen et al., 2013)
HOMA-IR			> 3.16	(Keskin et al., 2005)
Systolic/diastolic blood pressure	< 90th percentile	≥ 90th and < 95th percentile	≥ 95th percentile	(NHBPEP, 2004)

TC; total cholesterol, LDL; low density lipoprotein, HDL; high density lipoprotein, TG; triglycerides, FBG; fasting blood glucose, ALT; alanine aminotrasferase, AST; aspartate aminotransferase, GGT; gamma glutamyl transpeptidase, CRP; C-reactive protein, IL-6; interleukin 6, ICAM; intracellular adhesion molecule, HOMA-IR; homeostatic model assessment for insulin resistance , IFG; impaired fasting glucose, mmol/L; millimole per litre, mU/L; milliunit per litre, mg/L; milligram per litre, pg/ml; picogram per millilitre, ng/ml; nanogram per millilitre, µg/ml; microgram per millilitre.

HOMA-IR for the participants was measured using the equation mentioned in section 6.1.1.5 above. The equation was based on the method developed by Matthews et al. (1985). HOMA-IR is a proxy for insulin resistance and is widely used in clinical settings and research with high reliability in determining insulin resistance (Keskin et al., 2005).There is still a debate about the appropriate cut off point for HOMA-IR with proposed values of ≥ 2.5 (Sharma et al., 2011, Madeira et al., 2008), ≥ 1.77 (Arshi et al., 2010) and > 3.16 (Keskin et al., 2005). Keskin et al. (2005) assessed insulin resistance in obese and nonobese adolescents (mean age 12.8 years) using three different methods namely HOMA-IR, fasting glucose/insulin ratio (FGIR) and quantitative insulin sensitivity check index (QUICKI). Keskin and colleagues found out that HOMA-IR was the most sensitive and most specific of the three methods and the cut off point for insulin resistance diagnosis was 3.16. Sharma et al. (2011) based their HOMA-IR cut off point calculations on a sample of obese and nonobese children (mean age 6.5 years), and Arshi et al. (2010) had their cut off value for HOMA-IR based on samples of asthmatic children. Therefore, the definition of insulin resistance in this thesis will depend on values of HOMA-IR > 3.16 (Keskin et al., 2005).

Assessment of lipid profile for the participants included fasting TG, fasting cholesterol, fasting LDL, and fasting HDL (table 5.1). Jolliffe et al. (2006) developed age and gender specific percentiles for lipoproteins and cholesterol starting from age 12 to 20 years. However, our participants were aged 10 to 14 years and it was not possible to use the these lipoprotein percentiles for the whole sample, therefore the reference values for these parameters were taken from the National Cholesterol Education Program with fixed cut off points for normal, borderline and high values regardless of gender and age (NECP Panel (1992).

Liver function tests were obtained in all participants and included ALT, AST and gGT. The upper limit for ALT and AST in adults differ between populations and differences exist between males and females (Sohn et al., 2013). However, in studies examining the prevalence of abnormal ALT, AST and gGT in adolescents, the most commonly used cut off points were > 40 U/L, > 40 U/L and > 35 U/L, respectively (Siest et al., 1975, Strauss et al., 2000, Schwimmer et al., 2005), therefore , these were the values that we used as cut off points in our study.

Markers of inflammation were assessed in all participants. Acute phase protein CRP (CRP) was measured and is considered a primary warning of atherosclerosis in the paediatric population as well as an indicator of the chronic inflammatory state associated with obesity (Pearson et al., 2003). Generally, normal and abnormal levels of CRP were

developed for the adult population (Pearson et al., 2003, Jaye and Waites, 1997), and some studies tested for normal range in healthy adults to be from 0.08 to 6.1 mg/L (Macy et al., 1997). In our study we used the cut off points set by the American Heart Association and Centre for Disease Control and Prevention (Pearson et al., 2003) (see table 5.1).

The inflammatory cytokine IL-6 has an age-related variability with peak physiological elevation around age 4 and 15 years in relation to cartilage and bone development (Sack et al., 1998). In the literature, precise reference range for IL-6 vary greatly depending on the age and gender of the participants tested (Warnberg et al., 2004, Sack et al., 1998, Yamamura et al., 1998). However, several papers included values that have been extrapolated for healthy subjects within the study population (Sekiyama et al., 1994, Yamamura et al., 1998, Warnberg et al., 2004). As mentioned earlier, IL-6 level increases with obesity, and since our study population only included obese adolescents, we used the reference range of the control group (healthy controls n=37) from a study by Makni et al. (2013) where they examined the prevalence of a number of cardiometabolic risk factors in obese and non-obese Tunisian adolescents (mean age of the control group 13.7 years). The cut off point for abnormal value in the present study was > 3.9pg/ml.

Inflammatory plasma soluble adhesion molecules ICAM were also measured in all of the participants for its relation to the chronic inflammatory state associated with obesity as mentioned before. The literature shows that their reference value is age related and when applying the cut off point for our study we chose a study done in the Czech Republic by Andrys et al. (2000) to establish reference range for serum soluble adhesion molecules in healthy children and adolescents aged 6 to 15 years defined by values between the 5^{th} and 95^{th} percentiles for each inflammatory marker. The normal cut off range for 6 to 10 years old was 206.8-486.8 ng/ml, and for 11 to 15 years old was 184.1 to 355.0 ng/ml (Andrys et al., 2000).

The anti-inflammatory adipokine adiponectin was measured in all participants in the fasting state. It is normally present in plasma concentrations of 2-20 µg/ml(Oh et al., 2007). Most studies comparing adiponectin concentration in obese adolescents to its concentration in healthy controls referred to" low levels" when adiponectin concentration was < 5 µg/ml as compared to its concentration in healthy control subjects at > 10 µg/ml (Goksen et al., 2013, Tascilar et al., 2011, Alikasifoglu et al., 2009). Therefore, in the present study we used the same cut off points.

Hypertension was defined as a systolic and or diastolic blood pressure at or above the 95^{th} percentile or higher for age, sex and height measured on 3 separate occasions (NHBPEP,

2004). In order to fulfil the 3 separate occasions condition of the definition, blood pressure was measured before clinical consultation started, during the consultation and at the beginning of the physical examination of the clinical assessment interview.

5.2.6 Metabolic syndrome definitions

Metabolic syndrome was defined according to both the International Diabetes Federation (IDF) (Zimmet et al., 2007) and the National Cholesterol Education Programme Adult Treatment Panel III (ATP III) (Panel, 2001). Choosing these two definitions was based on the fact that both definitions share the same five parameters used in the diagnosis of MS namely: high waist circumference, high TG, low HDL, high blood pressure and high FBG (table 5.2). However, the IDF definition requires the presence of high waist circumference plus two or more of the 5 parameters and ATP III definition requires the presence of three or more of the 5 parameters. Table 5.2 shows the cut-off points for MS diagnosis by both IDF and ATP III.

Table 5.2 Cut off points of the International Diabetes Federation (IDF) and Third Adult Treatment Panel (ATP III) criteria

Factors	IDF criteria[1]	ATP III criteria[2]
Waist circumference (cm)	≥ 90th percentile or adult cut-off if lower	≥ 90th percentile
TG (mmol/L)	≥ 1.7	≥ 1.24
HDL (mmol/L)	< 1.03	≤ 1.03
Blood pressure (mmHg)	≥ 130/85	≥ 90th percentile
Glucose (mmol/L)	≥ 5.6	≥ 6.1

[1]IDF criteria for metabolic syndrome is the presence of high waist circumference plus two or more of the listed factors

[2]ATP III criteria is the presence of three or more of the listed criteria

5.3 Results

5.3.1 Characteristics of study participants

Table 5.3 shows the mean and SD of all measured parameters for the participants (n=80), for the boys (n=40), and for the girls (n=40). The mean age was 12.3 years (SD 1.1). These are the same participants as studied in the NATTO trial described in chapter 2, but the cardiometabolic risk factor data are based on baseline, pre-intervention blood samples. All participants were obese and had their BMI $\geq 95^{th}$ percentile for age and sex according to US CDC reference population (Kuczmarski et al., 2000).

5.3.2 Blood pressure

Twenty six out of the 80 participants (32.5%) had systolic and/or blood pressure at or above the 95th percentile for age, sex and height.

5.3.3 Fasting blood glucose, insulin, and HOMA-IR

Hyperglycaemia and hyperinsulinaemia was present in 2.5% (2/80) and 43.8% (35/80) of participants, respectively. Insulin resistance as defined by HOMA-IR value > 3.16 (Keskin et al., 2005) was found in 67.5% (54/80) of participants.

5.3.4 Lipid profile

Out of the 80 participants, 27.5% (22/80) had high TG level, 33.8% (27/80) had high total cholesterol level, 20% (16/80) had low HDL level, and 35% had high LDL level.

5.3.5 Liver function tests

Liver function tests showed high ALT in 26.3% (21/80) of participants, high AST in 88.8% (71/80) of participants, and high GGT level in 17.5% (14/80) of participants.

5.3.6 Inflammatory markers

Inflammatory markers included CRP, IL-6, ICAM and adiponectin as noted above. CRP level was high in 42.5% (34/80) of participants, IL-6 level was high in 7.5% (6/80) of participants, ICAM level was high in 66.3% (53/80) of participants and adiponectin level was normal in all participants.

5.3.7 Metabolic syndrome

Table 5.4 shows the results of waist circumference (WC), TG, HDL, FBG, systolic blood pressure and diastolic blood pressure using IDF and ATP III criteria. Seventeen of the 80 participants (21.3%) met the diagnosis of MS by the IDF definition and 24 of the 80 participants (30%) met the diagnosis of MS by the ATP III definition.

Table 5.3 Descriptive parameters of the adolescents according to gender, Mean (SD)

Variables	All Participants (n=80)	Boys (n=40)	Girls (n=40)	Number of participants with abnormality (%)	
				Borderline	High
Age, years	12.3 (1.1)	12.4 (1.2)	12.3 (1.1)	na	na
BMI Z score	2.2 (0.3)	2.2 (0.3)	2.2 (0.3)	na	na
Waist circumference, cm	93.3 (12.2)	96.6 (12.4)	90.0 (11.2)		
Systolic blood pressure, mmHg	122 (11)	125 (11)	119 (9)	na	24 (30.0%)
Diastolic blood pressure, mmHg	77 (8)	78 (8)	77 (7)	na	14 (17.5)
Total cholesterol, mmol/L	4.7 (0.9)	4.7 (1.0)	4.7 (0.8)	25 (31.5%)	27 (33.8%)
LDL, mmol/L	3.0 (0.8)	3.0 (0.9)	3.0 (0.7)	20 (25%)	28 (35.0%)
TG, mmol/L	1.3 (0.5)	1.3 (0.5)	1.3 (0.5)	26 (32.5%)	22 (27.5%)
HDL, mmol/L	1.1 (0.2)	1.1 (0.2)	1.1 (0.3)	60 (75%) low	16 (20.0%)
FBG, mmol/L	4.7 (0.8)	4.8 (0.9)	4.5 (0.6)	na	2 (2.5%)
Fasting insulin, µU/L	26.7 (23.8)	26.4 (25.8)	27.0 (22.0)	21 (26.5%)	35 (43.8%)
HOMA-IR	6.0 (7.3)	6.4 (9.2)	5.5 (5.0)	na	54 (67.5%)
ALT , U/L	34.2 (23.6)	42.2 (21.3)	26.1 (23.4)	na	21 (26.3%)
AST, U/L	58.1 (19.3)	63.3 (15.6)	52.8 (21.4)	na	71 (88.8%)
GGT, U/L	27.0 (12.6)	31.4 (13.9)	22.7 (9.6)	na	14 (17.5%)
CRP, mg/L	4.2 (5.1)	5.0 (4.6)	3.5 (5.5)	31 (38.5%)	34 (42.5%)
IL-6, pg/mL	2.0 (1.8)	1.9 (1.5)	2.0 (2.1)	na	6 (7.5%)
ICAM, ng/mL	461.3 (158.5)	493.2 (158.0)	429.4 (154.6)	na	53 (66.3%)
Adiponectin, ng/mL	50.7 (25.0)	47.0 (21.5)	54.4 (27.9)	na	none

LDL; low density lipoprotein, TG; triglycerides, HDL; high density lipoprotein, FBG; fasting blood glucose, ALT; alanine aminotransferase, AST; aspartate amino transferase

GGT; gamma glutamyl transpeptidase, CRP; C-reactive protein, IL-6; interleukin-6, ICAM; intracellular adhesion molecule, na; not applicable

Table 5.4 Metabolic syndrome prevalence using International Diabetes Federation (IDF) and Third Adult Treatment Panel (ATP III) criteria in the participants

Anthropometric and biochemical variables	Mean (SD)	IDF	ATP III
Waist circumference (cm)	93.3 (12.2)	66 (82.5%)	66 (82.5%)
TG (mmol/L)	1.3 (0.5)	12 (15%)	37 (46.5%)
HDL (mmol/L)	1.1 (0.2)	26 (32.5)	26 (32.5%)
FBG (mmol/L)	4.7 (0.8)	4 (5%)	2 (2.5%)
Systolic blood pressure	122 (11)	9 (11.5%)	11 (13.5%)
Diastolic blood pressure	77 (8)		
MS prevalence		17 (21.3%)	24 (30%)

TG; triglycerides, HDL; high density lipoprotein, FBG; fasting blood glucose.

5.4 Discussion

The current study is the first to estimate the prevalence of cardiometabolic risk factors and MS, using IDF and ATP III criteria, in a group of obese Kuwaiti adolescents.

The main findings of this study were the high prevalence of multiple cardiometabolic risk factors; out of the sixteen risk factors measured, eight were high in ≥ 30% of the participants (table 5.3). The cardiometabolic risk factors with highest prevalence of abnormal values included AST (88.7% of the sample), HOMA-IR (67.5% of the sample), ICAM (66.5% of the sample), fasting insulin (43.5% of the sample), CRP (42.5% of the sample), LDL (35.0% of the sample), cholesterol (33.5% of the sample), and systolic blood pressure (30.0% of the sample); 96.3% (77/80) of participants had at least one impaired cardiometabolic risk factor as well as obesity.

In clinical terms, most of the participants in our study had impaired lipid profile, insulin resistance, impaired liver function tests and chronic inflammatory process with high risk of atherosclerosis.

As demonstrated in chapter 6, most of the participating families had poor attendance at treatment intervention and to the control primary care condition. Therefore, findings from the present study, had they been available at the time the trial started, may have had an impact on compliance with the intervention, or at least on attendance. It might have been possible to use the cardiometabolic risk factor results to demonstrate to the adolescents and their families that their obesity was a medical problem which was affecting them, and so possibly persuade them to engage more with treatment. Moreover, all of the measured parameters in the present study, except for adiponectin, are readily accessible by physicians working in the Ministry of Health-Kuwait in the clinical setting, and are widely

available in many other parts of the world, so their measurement could be part of any treatment protocol for adolescent obesity in the future.

Risk factors for cardiovascular disease and type 2 diabetes mellitus have extended their roots to reach children and adolescents (Poyrazoglu et al., 2014, Herouvi et al., 2013, Beauloye et al., 2007, Weiss and Caprio, 2005, Reilly et al., 2003, Visser et al., 2001, Srinivasan et al., 1996, Strong et al., 1992). There are a number of studies that demonstrated this from the local and the international communities. Locally, Al-Isa et al. (2010c) have examined the prevalence of multiple circulating inflammatory biomarkers namely; CRP, ICAM, vascular cell adhesion molecule (VCAM), and HOMA-IR. They aimed at setting reference ranges of these markers in a group of 774 Kuwaiti adolescents aged 10 to 19 years. They also set the age 14 as the cut off point for puberty, due to social and cultural obstacles faced in Tanner staging their study sample. However, the sample included lean, overweight and obese boys and girls, classified according to the IOTF classification of obesity (El-Ghaziri et al., 2011, Cole et al., 2000), and knowing that obesity is an independent risk factor for cardiovascular disease, we rejected the use of their proposed reference ranges of the inflammatory biomarkers examined in our study. Moreover, taking reference ranges from a random sample in a population of high prevalence of paediatric obesity (El-Ghaziri et al., 2011) is most likely to be false positive. Having said that, the reference range for CRP in Al-Isa et al. (Al-Isa et al., 2010c) study was lower than what we used as cut off value in the present study. Using Al-Isa and colleagues proposed reference ranges in the present study increased the prevalence of participants with abnormal CRP from 42.5% (34/80) to 86.3% (69/80), decreased the prevalence of participants with abnormal fasting insulin from 43.8% (35/80) to 16.3% (13/80), and decreased the prevalence of participants with abnormal HOMA-IR from 67.5% (54/80) to 11.3% (9/80). The prevalence of participants with abnormal ICAM stayed the same (66.3%, 53/80).

On the other hand, they (Al-Isa et al., 2010c) concluded that ICAM, VCAM, CRP, and insulin resistance represented by HOMA-IR increase with increasing BMI and with age (< 14 or ≥ 14).

In a study from Iran (Kelishadi et al., 2013) on 5,528 adolescents aged 10 to 18 years assessing the relationship between multiple cardiometabolic risk factors (total cholesterol, TG, LDL, HDL, blood pressure and FBG) with BMI, low physical activity and unhealthy diet. BMI had the greatest direct effect on total cholesterol, LDL, TG, FBG and blood

pressure and an inverse relationship with HDL, more than that contributed by inactivity and unhealthy diet. Kelishadi et al. (2013) called for immediate interventions to tackle paediatric obesity and its associated cardiometabolic risk factors in order to prevent future risk of MS and chronic non-communicable diseases in Iran.

Kardas et al. (2013) compared the level of cholesterol, LDL, TG, HDL, FBG, blood pressure, vitamin D and adiponectin between obese (n=63) and nonobese (n=51) Turkish adolescents aged 10 to 16 years. Obesity was defined as BMI >90th percentile for age and gender specific Turkish reference population. Cholesterol, LDL, TG, FBG, blood pressure were significantly higher in the obese group compared to the nonobese group. Adiponectin, vitamin D, and HDL were significantly lower in the obese group compared to the nonobese group. Mean adiponectin value for the obese group was 3.3 (± 0.89) ng/ml and in the non-obese group the mean value was 6.0 (±1.4) ng/ml.

In the Netherlands, inpatient children and adolescents (n=80, aged between 8 to 19 years) diagnosed with severe obesity were evaluated for the presence of multiple cardiometabolic risk factors namely blood pressure, fasting insulin, FBG, HOMA-IR, cholesterol, LDL, TG, HDL and CRP (Makkes et al., 2013), as part of an inpatient treatment trial for their obesity. Data from the study (Makkes et al., 2013) showed that 80% of the participants had at least one impaired cardiometabolic risk factor as well as severe obesity. In comparison with our study, 90% of our participants had at least one impairment with regards to the same cardiometabolic risk factors assessed.

Aminotransferases are proxy markers for NAFLD. Our study showed that ALT and AST were elevated in 26% and 71% of participants, respectively. In a study done in Germany on 224 healthy, overweight and obese 1 to 12 years old children and adolescents, elevated liver enzymes (ALT, AST, GGT) were present in 29% of overweight and obese participants (Engelmann et al., 2014). An expert committee recommendation regarding the prevention, assessment, and treatment of child and adolescent overweight and obesity suggests biannual screening for liver disease with serum ALT and AST starting at age 10 years in obese children and adolescents (Barlow, 2007). However, no recommendation for NAFLD screening has been made by gastroenterology societies that jointly claimed more firm evidence is required before making any official recommendation (Chalasani et al., 2012).

We also noted in our main findings of the present study that the prevalence of metabolic syndrome was high, as almost third of the participants had MS, and prevalence varied

depending on the definition used. When using the IDF criteria (Zimmet et al., 2007) for definition of MS, 21.3% of our participants had MS, and 30% had MS according to the ATP III definition (Panel, 2001). In a study done in Kuwait on apparently healthy female adolescents (n= 431, age 10 to 19 years) to assess the prevalence of MS using the same definitions that we applied to our study, it was found that MS was present in 9.1% by ATP III definition and 14.8% had MS when IDF definition was used (Al-Isa et al., 2010a). In Saudi Arabia, the prevalence of MS using the IDF definition was high (18%) among 180 obese 9 to 12 year olds (Abdel-Megeid and Alfawaz, 2012). Also using the IDF definition in Lebanese adolescents, Nasreddine et al. (2012) found that 21.2% of the 104 obese adolescents (mean age 16 ±1.3 years) had MS, 3.8 % of the 78 overweight adolescents (mean age 16.4 ±1.4 years) had MS, and 1.2% of the 81 healthy-weight adolescents (mean age 16.8 ±1.3 years) had MS. In Iran, according to ATP III definition, MS has been found in 3.3% of Iranian adolescents (n=450, 15 to 18 years old) (Mehrkash et al., 2012). In a sample of 321 overweight, obese and extremely obese adolescents from Brazil (obesity defined using the CDC 2000 definition (Kuczmarski et al., 2000), MS was found in around 18% of the 10 to 16 year old adolescents using the IDF definition (Rizzo et al., 2013). Similarly in the USA (Weiss et al., 2004), it was found that > 50% of obese children and adolescents (n=439, 4 to 20 years old) had MS according to definitions modified from ATP III and WHO (Alberti and Zimmet, 1998).

Our participants were generally a fairly homogenous group of Kuwaiti adolescents, living in Kuwait City and recruited from 3 state schools, who were examined for the presence of cardiometabolic risk factors including metabolic syndrome. The use of traditional markers for cardiovascular disease i.e. lipid profile and blood pressure, multiple markers for inflammation i.e. CRP, IL-6 and ICAM, and for the first time adiponectin in a sample of Kuwaiti adolescents, assessment of insulin resistance as well as liver function, all add to the novelty of our study.

However, our study had a number of limitations. First, at general examination, Tanner staging of puberty was not possible to conduct due to social/ cultural and practical reasons. The clinical examination room assigned for the team was under-equipped (Appendix 3) with no available privacy screen therefore undressing the participants was not possible. As mentioned earlier this study was intended to be a baseline blood assessment in a RCT of treatment intervention for adolescent obesity in Kuwait (chapter 6), with an end of trial blood assessment to follow (after 6 months, at the end of the intervention). However, only a baseline assessment of cardiometabolic risk factors was possible. The Director of the

Laboratory Department in the Ministry of Health in Kuwait (i.e. the direct authorising personnel) refused to give the author access to the lab after 6 months and so blood based measures at the 6 month follow up were not possible (chapter 7). A similar obstacle was faced with schools' head principals in another follow up study of our quality of life assessment in obese and nonobese Kuwaiti adolescents (chapter 4). Having no follow-up data limited our analyses, and highlights the lack of interest in research within some authorities in Kuwait.

Nonetheless, we believe that our study highlights the importance of assessing multiple cardiometabolic risk factors in obese adolescents in Kuwait at a larger scale. Also we signify the importance of addressing the possible presence of these cardiometabolic risk factors and MS in obese Kuwaiti adolescents when conducting future treatment interventions – the relatively high prevalence of abnormal values for cardiometabolic risk factors could be a useful aid to engage more families into participating in treatment, and might also increase the level of commitment to participation by those who do take part (chapter 6).

5.5 Conclusions

The present study suggests that a number of cardiometabolic risk factors and metabolic syndrome are prevalent in obese Kuwaiti adolescents. This observation might provide impetus to future strategies to treat paediatric obesity, and to prevent or delay the appearance of cardiovascular disease and diabetes mellitus in the future adult generation. The observation might also be used to encourage greater engagement with treatment among families, and might also help persuade some of the authorities in Kuwait that such studies are valuable and necessary.

6. Results of the National Adolescent Treatment Trial (NATTO) Randomised Controlled Trial

BOODAI, S. A., MCCOLL, J. H. & REILLY, J. J. In press. Randomised controlled trial of a good practice approach to treatment of adolescent obesity in Kuwait: National Adolescent Treatment Trial for Obesity in Kuwait (NATTO): Project design and results. Trials. Appendix F.

6.1 Introduction

This chapter outlines the results of the NATTO study (Boodai et al., 2014b) which assessed the feasibility and efficacy of a trial of a family based behavioural treatment programme for obese adolescents in Kuwait compared to primary care in respect to primary and secondary outcomes. The rationale for this study was described fully in chapter 1, the trial design and methodology were described fully in chapter 2, and the intervention manual was described fully in chapter 3.

Despite the high prevalence of childhood and adolescent obesity and its associated medical and psychological consequence, treatment interventions have only been modestly successful in creating change in the targeted behaviours and typically show short term effects (Oude Luttikhuis et al., 2009). Moreover, the recent Cochrane review (Oude Luttikhuis et al., 2009) found only 29 eligible trials of adolescent obesity treatment, and none of these were from the Arab world (16 from North America, 7 from Europe and Australia; 3 from Far East Asia; 2 from Israel). At present the availability of treatment for obese adolescents in Kuwait is negligible.

The primary aim of the present study was therefore to test the hypothesis that a ‘good practice’ intervention for the treatment of adolescent obesity in Kuwait would have a greater effect on primary and secondary outcomes than allocation to a control group. The secondary aims were to test the feasibility of conducting such a trial in Kuwait, and the feasibility of using a good practice intervention and referral to primary care as a control condition, with a view to developing improved obesity treatment RCT in Kuwait and the other Gulf States.

6.2 Methods

6.2.1 Power calculations

Data analysis was carried out using Minitab 16. The author carried out the analysis presented in this chapter with the advice of Professor John McColl, Department of Statistics, University of Glasgow.

As discussed in chapter 2, the primary outcome measure for the study was change in BMI Z score from baseline to six months and the study had been powered for 30 participants in each arm at 6 months with change in BMI Z score of -0.25 between groups with 90% power at 0.05 significance.

6.2.2 Study participants

Participating subjects had to meet the inclusion criteria. These criteria were discussed in detail in chapter 2 and included, age 10-14 years, Obese (BMI $\geq 95^{th}$ percentile relative to US reference data), have at least one parent willing to participate in the trial.

A total number of 224 obese adolescents were assessed for eligibility for the present study; 82 consented and were recruited into the study; 41 participants were randomised to the primary care control group (boys 51%) and 41 to the intervention programme (boys 51%). Of the 82 participants entered at baseline, 63 (77%) participants (31 from the intervention group and 32 from the control group) were available for the six month follow-up. The expected drop out rate as decided in SCOTT's power calculation was 36% at 6 months. The actual drop-out rate at 6 months was 23%. Figure 4.1 shows the CONSORT 2010 (Moher et al., 2012) flow diagram of the participants throughout the study.

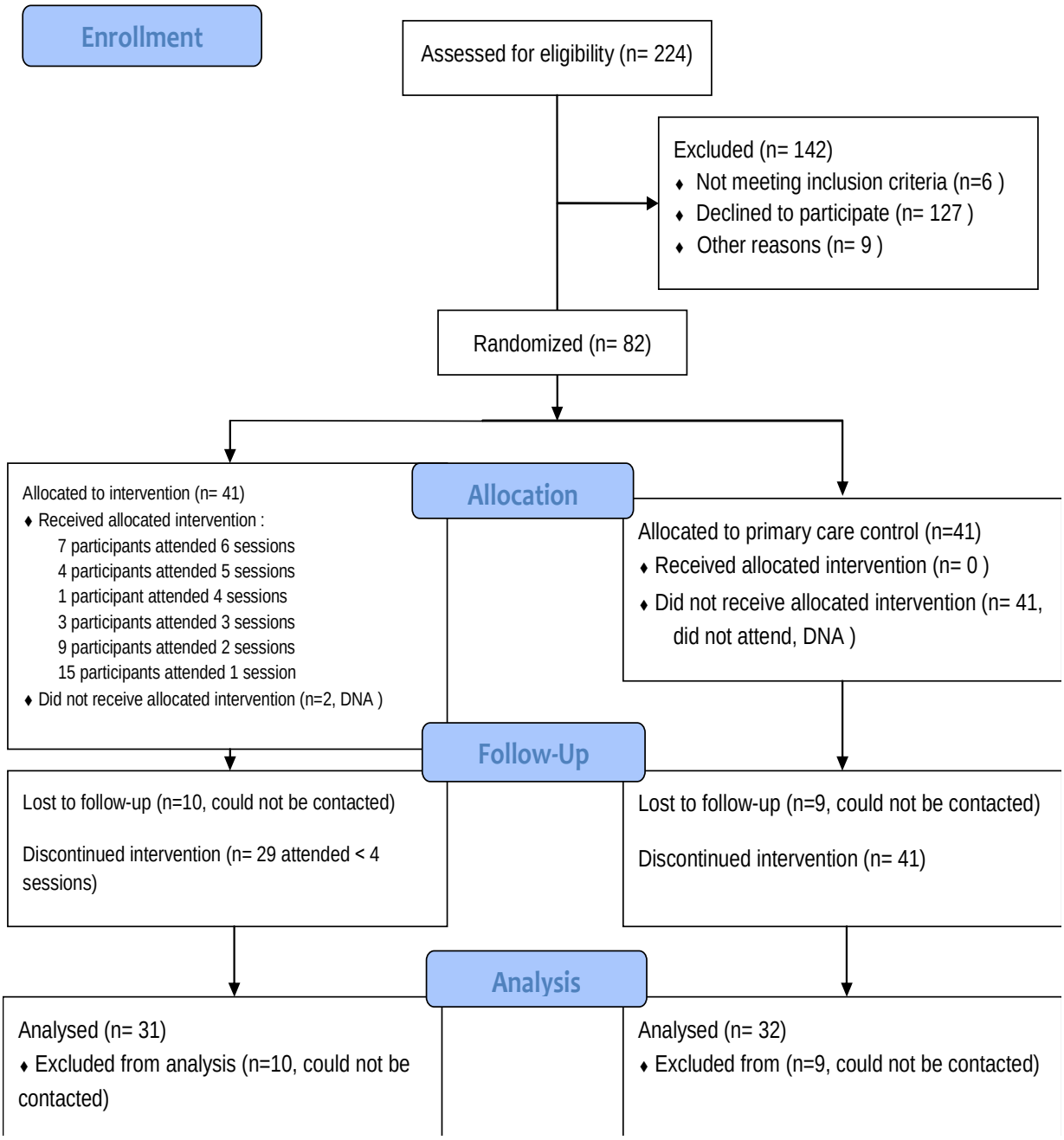

Figure 6.1 CONSORT 2010 flow diagram for NATTO

6.2.3 Data analysis

Primary and secondary outcome measures were tested for normality by comparing the means and medians and using Ryan Joiner Normality Tests (a normal distribution was assumed if $p \geq 0.05$). Appendix 2 shows the normal distribution curves for the physical, psychological and total scores. Most outcome measures were normally distributed. Therefore, all data within this chapter are reported as mean and standard deviation; the parametric tests (paired t-test and 2- sample t-test) were used. Changes in variables from baseline to six months follow up for each participant within the group were tested using paired t-test. Changes in outcome variables between groups, i.e. intervention and control groups were examined using 2- sample t-test. A p value of < 0.05 was taken to indicate statistical significance.

As described in chapter 2, intention to treat (ITT) analysis was used- this involved including all subjects for whom data were available regardless of their attendance. Missing data were excluded from the analysis.

The baseline characteristics of participants include age, gender, and anthropometry. Reporting of baseline demographic profiles and other characteristics of each group in NATTO study is a requirement of the CONSORT statement of RCT (Moher et al., 2012). Socioeconomic status of participants is also a requirement, and in the UK for example, a relatively precise definition of social class based on the general social standing of the occupation of the person suggested by the Registrar General is widely used (Coombs et al., 2013). In Kuwait however, there is no official definition of socioeconomic status (Shah et al., 1999). Also, there is no consensus among researchers in Kuwait on how to define social class in this community (Shah et al., 1999). On the other hand, the Capital; where the trial is conducted, is considered the most highly developed residential area in Kuwait and Kuwaiti nationals have a high standard living. There are other means to measure socioeconomic status (SES) such as parents' education, occupation, income, and type of housing, but the author did not carry out this survey as all participants were selected from schools in the Capital and further inquiry into the SES was judged to be time consuming and not feasible.

Eight participants (19%) from the intervention group (n=41) attended 100% of the treatment sessions; that is 6 sessions. None of the control group attended any of the primary care appointments; only four parents arranged for appointments, however, none of

these actually attended any sessions in primary care. As a result of low compliance with the intervention, per protocol analysis for BMI Z score was not performed.

6.3 Results

6.3.1 Subject recruitment and group allocation

A total n of 224 obese adolescents were assessed for eligibility for the present study as described earlier (See Fig. 4.1); 142 families were excluded due to the following reasons:

A. 6 families did not meet the inclusion criteria due to medical history.
B. 127 families with eligible adolescents refused to participate due to lack of interest and time.
C. 9 families failed to attend the baseline assessment clinic appointment and were not enrolled in the study.

Therefore the final sample size consisted of 82 families, which represented 37% of inquiries from the eligible families; 41 participants were randomised to the control group (primary care) and 41 to treatment group (intervention).

Of the 82 participants entered at baseline, 63 (77%) of participants (32 from the control group and 31 from the intervention group) attended the six month follow up.
The expected drop out rate from power calculation was 30%, however, the actual drop-out rate for the present study at six months was 23%.

6.3.2 Adherence to treatment intervention

Programme session attendance was used as a proxy measure for adherence to the study protocol. Better attendance to treatment sessions has been associated with improved clinical outcomes and prevention or reduction of complications (Wadden et al., 2005, Chao et al., 2000). Of the 41 intervention group participants, 12 (29%) participants attended 4 out of the 6 treatment sessions and 29 (71%) participants attended less than 4 treatment sessions.

6.3.3 Characteristics of participants at baseline

The baseline characteristics of the two study groups were similar and these are shown in table 4.1. There were 21 boys and 20 girls in both the intervention group and the control group. There were no significant differences between the groups for age, blood pressure, and anthropometric measures (table 6.1).

Table 6.1 Baseline characteristics of the study participants

Variable	Intervention group (n=41)	Control group (n=41)	*p* value[1]	Whole sample (n=82)
Age (years)	12.4 (1.2)	12.4 (1.2)	0.9	12.4(1.2)
Male / Female	21 / 20	21 / 20		42 / 40
BMI Z score	2.2 (0.3)	2.2 (0.3)	0.2	2.2 (0.3)
% Body Fat	43.3 (7.3)	44.7 (6.9)	0.4	44.0 (7.1)
Systolic BP (mm Hg)	122.0 (12.3)	122.0 (8.2)	0.9	122.2 (10.4)
Diastolic BP (mm Hg)	76.0 (8.5)	79.1 (6.4)	0.1	77.5 (7.6)
Waist circumference (cm)	93.0 (12.7)	94.0 (11.6)	0.7	93.5 (12.1)

Data are mean (SD), BP = blood pressure, [1]2-sample t-test

6.3.4 Primary outcome- change in BMI Z score

Changes within groups

The primary outcome of the NATTO study was change in BMI Z score from baseline to six months. Table 6.2 shows the changes in BMI Z score from baseline to six months (mean and SD, paired t-test). The analysis included all subjects with available measures at six months post baseline (intervention group n=31, control group n=32). There was no statistically significant difference within each group for BMI Z score at any measurement point.

Table 6.2 Change in BMI Z score within group over time, Mean (SD)

Group (n)	Baseline	Six months	*p* value[1]
Intervention (31)	2.2 (0.3)	2.2 (0.3)	0.5
Control (32)	2.2 (0.3)	2.2 (0.3)	0.3

[1]Paired t-test by group

Differences in change in anthropometry between groups

As mentioned earlier, the aim of the NATTO study was to test for changes in BMI Z score from baseline to six months and the study had been powered on a change in BMI Z score of -0.25 at six months. Table 6.3 shows the change in BMI Z score from baseline to six months (2-sample t-test) compared between the intervention group and the control group. The analysis was conducted for all subjects with available measures at six months post baseline (intervention group n=31, control group n=32). There was no significant difference in the between group change in BMI Z score at six months.

Therefore, our hypothesis that the office-based intervention would be more successful in reducing BMI Z score than the control group was rejected.

Table 6.3 Change in BMI Z score between groups over time, Mean (SD)

Period	Intervention group n=31	Control group n=32	Between group change *(95% CI)	*p* value[1]
from 0 to 6 months	0.0 (0.1)	0.0 (0.2)	0.0(-0.1; 0.1)	0.6

* 95% Confidence Interval, [1] 2-sample t-test

6.3.5 Secondary outcomes

6.3.5.1 Changes in percentage body fat (%BF)

Changes within groups

Percentage body fat decreased significantly within each group over the six month period of the trial ($p < 0.001$, respectively) (table 6.4).

Table 6.4 Change in percentage body fat within group over time, Mean (SD)

Group (n)	Baseline	Six months	*p* value[1]
Intervention (31)	43.8 (7.0)	41.0 (6.0)	<0.001
Control (32)	44.2 (7.5)	40.9 (7.3)	<0.001

[1]Paired t-test by group

Changes between groups

Although each group (intervention n=31 and control n=32) had a statistically significant drop in percentage body fat over six months, the difference between groups as tested by 2-sample t-test was statistically insignificant (p 0.6) (table 6.5).

Table 6.5 Change in percentage body fat between groups over time, Mean (SD)

Period	Intervention group	Control group	Between group	*p* value[1]

	n=31	n=32	change *(95% CI)	
From 0 to 6 months	-2.8 (3.7)	-3.4 (4.1)	-0.5 (-2.5; 1.4)	0.6

* 95% Confidence Interval, [1]2-sample t-test

6.3.5.2 Changes in blood pressure

Changes within groups

Examination of change in systolic blood pressure from baseline to six months within each group via paired t-test revealed no significant differences in the means (table 6.6).

Table 6.6 Systolic blood pressure (mmHg) within group over time, Mean (SD)

Group (n)	Baseline	Six months	*p* value[1]
Intervention (31)	122.0 (13.0)	122.0 (10.0)	0.8
Control (32)	122.0 (8.0)	123.0 (7.0)	0.5

[1]Paired t-test by group

There was a statistically significant increase in diastolic blood pressure within the intervention group (p 0.01) at six months. Difference in diastolic blood pressure at six months post baseline for the control group was not statistically significant (*p* 0.3) (table 6.7).

Table 6.7 Diastolic blood pressure (mmHg) within group over time, Mean (SD)

Group (n)	Baseline	Six months	*p* value[1]
Intervention (31)	76.0 (9.0)	79.0 (7.0)	0.01
Control (32)	79.0 (7.0)	80.0 (5.0)	0.3

[1]Paired t-test by group

Changes between groups

Table 6.8 shows the mean and SD of changes in systolic blood pressure between the intervention group (n=31) and the control group (n=32) from point 0 to six months. Using 2-sample t-test, the analysis showed that there was no significant difference change in systolic blood pressure over time between the intervention and the control groups (p 0.9).

Table 6.8 Change in systolic blood pressure (mmHg) between groups over time, Mean (SD)

Period	Intervention group n=31	Control group n=32	Between group change *(95% CI)	p value[1]
From 0 to 6 months	0.4 (6.7)	0.6 (4.8)	0.3 (-2.7; 3.2)	0.9

* 95% Confidence Interval, [1]2-sample t-test

Table 6.9 shows the difference in diastolic blood pressure from baseline to six months between the intervention group (n=31) and the control group (n=32) which was statistically insignificant.

Table 6.9 Change in diastolic blood pressure between groups over time, Mean (SD)

Period	Intervention group n=31	Control group n=32	Between group change *(95% CI)	p value[1]
From 0 to 6 months	2.9 (6.2)	1.1 (5.8)	-1.8 (-4.8; 1.3)	0.2

* 95% Confidence Interval, [1]2-sample t-test

6.3.5.3 Changes in waist circumference

Changes within groups

Both the intervention group and the control group had a statistically significant increase in waist circumference measurement from baseline to six months (table 6.10).

Table 6.10 Waist circumference (cm) by group over time, Mean (SD)

Group (n)	Baseline	Six months	p value[1]

Intervention (31)	94.0 (13.7)	98.9 (14.6)	<0.001
Control (32)	92.3 (11.1)	95.7 (12.5)	<0.001

[1]Paired t-test by group

Changes between groups

There was no significant difference between the groups for change in waist circumference (*p* 0.3) (table 6.11).

Table 6.11 Change in waist circumference (cm) between groups over time, Mean (SD)

Period	Intervention group n=31	Control group n=32	Between group change *(95% CI)	*p* value[1]
From 0 to 6 months	4.9 (5.8)	3.5 (5.7)	-1.4 (-4.3; 1.5)	0.3

* 95% Confidence Interval, [1]2-sample t-test

6.4 Discussion

6.4.1 Summary of main findings

While it seems that no previous adolescent obesity treatment trials have been published from Kuwait or other Gulf States, the present study suggests that conducting randomised controlled trials of adolescent obesity treatment interventions in Kuwait is feasible. Feasibility examines the practicality of conducting research in terms of recruitment and retention. The study power calculation showed that approximately 30 participants were required in each arm at six months and in reality 31 participants from the intervention group and 32 participants from the control group attended the six months assessment. Retention level was acceptable and strikingly similar to that reported in other adolescent obesity treatment trials which took place over a similar time scale (Oude Luttikhuis et al., 2009). Luttikhuis and colleagues in the recent Cochrane review described drop-out in adolescent obesity treatment trials ranging from 0 to 43% at the end of intervention.

The primary outcome in the present study was BMI Z score and based on the SCOTT study power calculation we hypothesised that the intervention programme might be efficacious in reducing BMI Z score by approximately 0.25 over six months in the

intervention group to no change in the control group, and it is quite a small difference in BMI Z score as discussed below. Both paired t-tests and 2-sample t-tests revealed no significant difference in changes in BMI Z score within each group and between groups. The present study therefore failed to show that an office-based good practice obesity treatment programme could improve the primary treatment outcome.

Although mean BMI Z scores were essentially unchanged from baseline to six months in both groups, weight increased significantly in both groups ($p<0.00$ for both groups) with no significant difference in weight change between the groups (p 0.6).

Weight maintenance is widely recommended as an important aim of childhood and adolescent obesity treatment (SIGN, 2010, NICE, 2013). In the present study, 16% (6 out of 31) of those in the intervention group maintained or lost weight from baseline to six months. On the other hand, 15% (5 out of 32) of the participants in the control group had maintained or lost weight during the six month trial. This also indicates that the intervention programme was not superior to no-treatment option, and that treatment achieved relatively little in relation to treatment targets. In a recent review with meta-analysis on the effectiveness of lifestyle interventions in child and adolescent obesity (Ho et al., 2012) Ho and colleagues reported 18 out of 22 included studies to have positive effect on weight loss. In this analysis the included studies were of lifestyle interventions versus a no treatment or wait-list control group and the effect size varied by age of participants and length of study. Ho and colleagues also conducted a meta-analysis on 7 studies that reported BMI Z score as a primary outcome. Pooled BMI Z score reduction was 0.1 greater for lifestyle intervention compared with the control condition.
What represents a clinically meaningful reduction in BMI Z score with obesity treatment is unclear as noted by the SIGN guidelines in 2010 (SIGN, 2010) and this question has been debated in some studies (Kolsgaard et al., 2011, Reinehr et al., 2006, Reinehr and Andler, 2004). There is no agreed cut off point for the degree of reduction in BMI Z score which is desirable or the timescale over which the reduction in BMI Z score should be achieved, but improvements in cardiovascular disease risk factors have been associated with a reduction of 0.1 to 0.5 following treatment interventions (Kolsgaard et al., 2011, Reinehr et al., 2006). Unfortunately, in the present study, reductions of ≥ 0.1 of BMI Z score over six months were achieved by only 25% (8 out of 31) of the intervention group and 21% (7 out of 32) of the control group.

Accompanying the weight increase in both arms of the trial from baseline to six months was a significant increase in waist circumference in each group with no between-group differences. Waist circumference measurements were taken as indices of fat distribution, although the clinical meaning of this measurement in paediatric population is still unclear (Rudolf et al., 2007). The significant decrease in % body fat within the intervention and the control group at six months could be explained of being a result of linear growth. Details entered into impedance software for the end of trial assessment were different from baseline with regards to age and height. Height for both groups increased significantly at 6 months. The Tanita BIA software uses age, height and gender based proprietary formula to make the body fat estimate. However, the use of % body fat along with BMI Z score changes from baseline to end point of longitudinal studies can be useful tool in detecting group differences in fatness changes (Basterfield et al., 2012)

On a positive note, the present study intervention appeared to have had no negative impact on height or systolic blood pressure from baseline to six months. However, the classical approach for an intervention to have a negative impact on growth or general homeostasis of the body is usually with more intensive dietary management involving for example calorie restriction with subsequent nutrient restriction that could at the end result in greater weight reduction (SIGN, 2010, Rivera et al., 2003).

An evidence-based fourth report from the National High Blood Pressure Education Program (NHBPEP) working group on children and adolescents (2004) defines adolescent prehypertension as ≥120/80 mmHg and recommends rechecking blood pressure in 6 months with weight management counselling if overweight or obese. The issue of measurement error is acceptable in group level comparisons (e.g. intervention group vs control group) than for changes within individuals.
The mean systolic blood pressure at baseline for the whole sample was 122 mmHg (SD 10) and for diastolic blood pressure was 77 mmHg (SD 8). At 6 months assessment, the intervention group had a mean blood pressure of 122/79 mmHg (SD 10/7) where they has a statistically significant increase in their diastolic blood pressure (p 0.01) and the control group had their mean blood pressure at 123/80 (SD 7/5). It is evident that the whole sample had prehypertension from the beginning and it stayed with them through to the end of trial. Our intervention did not provide treatment for the intervention group and although diastolic blood pressure increased significantly, it remained within normal range and it is the systolic blood pressure that defined prehypertension for the whole sample.

6.4.2 Intervention feasibility

The NATTO intervention programme was designed to involve parents and their obese adolescents as recommended by evidence-based guidelines (SIGN, 2010, NICE, 2013). In the present study, consented parents and their adolescents were perceived to be motivated to participate. However, the trial records showed that attendance in both the intervention arm and the control arm were poor.

The intervention programme was originally designed to a total of 12 sessions arranged as one session every two weeks for 6 months. In the first session 36 families out of the 41 families attended. Two weeks after the author had to cancel the session due to cancellation by almost all families. This scenario was repeated for the session that followed and the author had to condense the sessions to 6 instead of 12 and to take place every month instead of every two weeks. Attendance was still poor and only 12 (29%) of participants attended 4 out of the 6 sessions.

Reasons behind poor attendance are largely anecdotal and not based on formal qualitative evaluation. The recent MRC Framework on developing and evaluating complex interventions (Craig et al., 2008) recommends that in order to explore reasons behind failed intervention attendance, qualitative studies should be run in conjunction with the intervention trial, but this was not possible for the present study due to lack of resources. The main reasons conveyed by parents for not attending were related to school work or simply forgetfulness, although the original study programme (12 sessions) and the amended programme (6 sessions) were provided to parents, and reminders were also provided for each upcoming session by means of phone calls and SMS. This suggests that reasons for not attending were not directly related to the study programme itself. Time and location were not among the list of reasons for non-attendance as described in a US weight management study (Barlow and Ohlemeyer, 2006). A recent review on the reasons behind high attrition rate in paediatric weight management studies suggested specific stigma describing the main characteristics of the participants with high attrition rate and these include: severe obesity; the presence of comorbidities; racial/ethnic minorities; poor or single-parent households (Skelton and Beech, 2011) none of which existed in the present study participants.

A better understanding of the obstacles, if any, behind parents' non-adherence to treatment sessions requires further exploration using qualitative methods, and goes beyond the scope of the present study.

The intervention programme was tested against the standard care which is an individualised clinic appointment with subsequent follow up. However, only four parents attempted to arrange primary care appointments and none of the participants in the control group attended any standard care sessions, as evident from the clinic formal records. Subsequently, the intervention programme was in effect tested against a no treatment control.

6.4.3 Declining interest in intervention

A total of 136 eligible families did not consent to participate in the study due to various reasons. The main reason given by the families was concern for their child's academic performance. Other anecdotal reasons for declining to participate were lack of interest and time, and unawareness of parents regarding their child's weight status. Some parents have actually challenged the author arguing that the children's weight was simply a result of puberty. Parental unawareness of their offspring overweight and obesity has been reported internationally (Parry et al., 2008) and in Kuwait (Al-Qaoud et al., 2010).

6.4.4 Comparisons with other studies

SCOTT was an RCT based in Scotland and targeted 5 to 11 year olds by means of generaliseable best practice individualised family centred behavioural intervention and since NATTO intervention was based on the SCOTT trial, a brief comparison with the outcomes of SCOTT is appropriate. Table 6.12 shows a comparison between SCOTT study results and NATTO.

The change in BMI Z score, physical activity levels and quality of life over time in the Hughes et al (Hughes et al., 2008) were reported as median (IQR), so the author used the mean (SD) results from Stewart thesis (Stewart, 2008). Also, Hughes et al (2008) reported results at 6 months end of treatment and at 12 month follow-up, but in the present study we only reported results at 6 months end of treatment.

Both studies show similar results in primary outcome at 6 months for the intervention groups and the control groups.

Table 6.12 Comparison of the present NATTO study with SCOTT study

	NATTO	SCOTT
Participants	10 to 14 years old, Kuwait n=82 (42 males) randomised; n=41 intervention group (IG) IG 6 months n=31 CG (control group) 6 months n=32 No 12 months follow up	5 to 11 years old, Scotland n=134 (59 males) randomised; n=69 Intervention group IG 6 months n=48, 12 months n=45 CG 6 months n=49, 12 months n=41
Primary outcome	Changes in BMI Z score at 6 months end of treatment	Changes in BMI Z score at 6 months end of treatment
Secondary outcomes	% body fat (%BF), Waist circumference (WC), blood pressure (BP) at 6 months (end of treatment)	Total activity + time in sedentary behaviour, light intensity + [1]MVPA at 6 months (end of treatment), measure of quality of life at 6 months (end of treatment)
Primary outcome at 6 months	IG 0.0 (0.1) CG 0.0 (0.2) Mean (SD)	IG -0.1 (0.2) CG -0.1 (0.2) Mean (SD)
Secondary outcomes at 6 months	%BF IG -2.9 (3.7) CG -3.4 (4.1) WC IG 4.9 (5.8) CG 3.5 (5.7) Systolic BP IG 0.4 (6.7) CG 0.6 (4.8) Diastolic BP IG 2.9 (6.2) CG 1.1 (5.8) Mean (SD)	Total activity (accelerometry [2]cpm); IG 18 (163) CG -98 (165) Sedentary behaviour; IG 0.1 (5.6) CG 3.8 (5.3) Light intensity ; IG -0.6 (4.6) CG -3.3 (4.1) MVPA; IG 0.5 (2.1) CG -0.4 (1.8) Quality of life, Total child report IG 3.7 (12.6) CG 6.9 (13.5) Total parent report IG 3.3 (9.1) CG 5.2 (9.8) Mean (SD)

[1]MVPA; moderate-vigorous physical activity, [2]cpm; count per minute, IG; intervention group, CG; control group

Several studies have tested intervention techniques for the treatment of adolescent obesity which ranged from exercise classes, education classes, dietary modification, inpatient therapy, cognitive behavioural therapy, to drug therapy (Oude Luttikhuis et al., 2009). Few group based educational programmes for the treatment of adolescent obesity were included in the most recent Cochrane review for obesity treatment in children and adolescents (Rodearmel et al., 2007, Nemet et al., 2005, Israel et al., 1994, Mellin et al., 1987). Rodearmel et al. (2007) America on the Move (AOM) intervention is an example of examining how providing minimum information regarding diet and physical activity could aid weight loss. It involved meeting the families during the intervention period of 6 months to alter two behaviours related to diet (replacing sugar with sweetener) and physical activity (walk additional 2000 steps per day using pedometer). Participants (n=218 age 7 to 14) were randomised to either the AOM group or the self-monitoring group (SM). AOM group received nutrition education and support around replacing dietary sugar and increasing their level of physical activity while the SM group were asked only to wear pedometers and record physical activity with no further guidance. The treatment sessions were held once per month for 6 months for the AOM group. Both groups had a statistically significant reduction in BMI Z scores at 6 months; however the difference between the groups was not significant. Another study (Nemet et al., 2005) was conducted in Israel and involved randomising 54 families (participants age 6 to 16 years) to either the intervention group or the routine care group. The intervention consisted of four evening lectures on childhood obesity, general nutrition, in addition to a balanced hypocaloric diet and twice weekly exercise programme. The study was held for 3 months and outcomes were measured at end of the intervention and again in 12 months. Outcomes measured included height, weight, BMI, skin-fold thickness and lipid profile. There was significant decrease in body weight, BMI and percentage body fat, cholesterol and LDL at 3 months and 12 months for the intervention group while the routine care group gained weight at 3 months and 12 months.

Another study from the USA conducted over 2 decades ago by Israel et al (1994) and included in the Cochrane review (Oude Luttikhuis et al., 2009, Israel et al., 1994). It tested behavioural treatment programme of obesity in which either parents had the primary responsibility to follow the programme (control group) or enhanced child involvement (ECI) condition (intervention group) which basically means giving the children some responsibility for self-management. Thirty four families were randomised and the age range of the children was 8 to 13 years. The programme lasted for approximately 6 months and involved weekly group discussions, homework assignments regarding stimulus

control, physical activity, food intake and rewards. End of treatment outcomes were percentage overweight (based on weight for age, height and sex), triceps skin-fold thickness and measures of self-regulation and self-control. There was significant reduction of %overweight in both the intervention and the control group. Mellin and colleagues (Mellin et al., 1987).

Recent paediatric obesity treatment studies also focus on cardiometabolic as well as weight management. A more recent systematic review and meta-analysis on the use of lifestyle interventions to treat childhood and adolescent obesity and/or improve the cardiometabolic outcomes conducted by Ho et al (2012). The systematic review included 38 RCTs that compared lifestyle interventions to no treatment/ wait list, usual care or written educational materials controls. The dietary component of the lifestyle interventions included traffic light diet or modified traffic light diet, or calorie restriction. Nineteen studies incorporated physical activity sessions. The results showed a statistically significant reduction in BMI Z score (-0.1, 95% CI -0.18 to -0.02) and when the intervention was longer than 6 months duration, greater weight loss was observed. There was also a significant improvement in LDL, TG, Fasting insulin and blood pressure. In our study, cardiometabolic risk factors were obtained at baseline, and there was an end of trial measurement to be made. However, due to bureaucratic complexity, end of trial measurement of cardiometabolic risk factors were not possible.

In 2013 Sbruzzi and colleagues published a systematic review and meta-analysis on the use of educational programmes with behavioural, nutritional and physical activity components, for the prevention and treatment of paediatric obesity (Sbruzzi et al., 2013). Eight studies were treatment trials and the outcomes included waist circumference, BMI and BMI Z score. The review showed that educational treatment interventions for at least 6 months resulted in significant reduction in waist circumference, BMI, BMI Z scores and diastolic blood pressure.

El-Sabban and Badr (2011) tested the nutrition knowledge of slightly older group than our sample (age 15 to 21 years 1,037 Kuwait University student) with regards to general nutrition, nutrition-related health problems and different groups of nutrients. The scores were poor, fair or good. The overall nutrition knowledge of the sample was rated as fair. One of our objectives in our study was to build up nutrition knowledge among the

intervention group in an attempt to correct the deficit in nutrition and health relationship that is evident from the El-Sabban and Badr study.

6.4.5 Study strengths and limitations

The principal strengths of the present study were: the high level evidence obtained, with adherence to the CONSORT statement on conduct and reporting of RCT (Moher et al., 2012); the fact that the trial was powered adequately, in contrast to a number of previous trials in this area (Oude Luttikhuis et al., 2009); development and testing of a potentially generalisable intervention; completing a challenging adolescent obesity treatment RCT (Warren et al., 2007) in the novel setting of a Gulf State.

At baseline, there were no significant differences between the study groups in terms of anthropometric measures, weight status, and blood pressure (table 6.1). This suggests that randomisation was successful in avoiding any discrepancies between groups at baseline.

The present study also had a number of weaknesses. Longer-term obesity treatment trials are desirable, and a 6 month follow up is considered the minimum desirable in the most recent Cochrane review of paediatric obesity treatment RCT (Oude Luttikhuis et al., 2009). An assessment of parent and adolescent perspectives on the treatment programme would have been desirable in order to both understand the current intervention better and to inform future treatment interventions (Craig et al., 2008, Stewart et al., 2008a, Murtagh et al., 2006). The intervention was designed to modify dietary, physical activity and sedentary behaviours, however, and the measured outcomes did not include an assessment of these behavioural measures. We did not have the time or human or equipment resource to make that assessment, however, weight and adiposity measure changes might give an indication as to whether any such behavioural change took place, though they could not identify what the behavioural changes were.

6.4.6 Study implications and suggestions for further research

This study addresses the need for serious efforts to address what seems to be the gap between treatment interventions and families. This patient-intervention interface needs further evaluation to identify reasons behind adherence and attrition. Qualitative studies should therefore be conducted in parallel with treatment intervention studies to help with quality control of the intervention tested and also help shape future treatment policy.

Future intervention trials in Kuwait might find it useful to focus treatment at other population subgroups (e.g. younger or older participants, or to tailor treatment to boys or to girls) or in other settings (e.g. a hospital or school based programme), but this was not possible in the present study due to resource limitations. Moreover, future studies should aim to assess behavioural changes in diet, physical activity and inactivity as part of the study's outcome.

6.5 Conclusions

The present study is the first reported intervention for the treatment of adolescent obesity in Kuwait. The study suggests that an adolescent treatment trial is feasible, but the intervention used seemed much less feasible and had no benefits in terms of clinically relevant reductions in BMI or other weight status measures. With the persistence of adolescent obesity, more randomised controlled trials of treatment interventions should be conducted in accordance with the high standards of the CONSORT statement with the support of the Kuwaiti authorities, parents and schools.

7. General Discussion

The current thesis set out to examine the feasibility and efficacy of an adolescent obesity treatment intervention in Kuwait. It also sought to explore the health related quality of life in obese adolescents and the prevalence of cardiometabolic risk factors, and whether these health related quality of life and cardiometabolic risk factors would change after completion of the treatment intervention.

There is general agreement in the literature that there is a lack of evidence from obesity treatment trials of adolescents, especially from the non-western world (Ho et al., 2012, SIGN, 2010, Oude Luttikhuis et al., 2009, NICE, 2013), and more recent evidence suggests that adolescents may be more resistant to obesity treatment than children (Danielsson et al., 2012). Danielsson and colleagues (2012) investigated the response of obese children and adolescents to 3 years of behavioural treatment intervention for obesity. From the 643 patients in their cohort, 20% of the adolescents of the age range 10 -13 years had what was considered to be a clinically significant reduction in BMI Z score of ≥ 0.5, while 58% of children at the age range 6-9 had reduction in BMI Z score of ≥ 0.5. Therefore, obese adolescents might be a particularly challenging group to treat, even outside Kuwait.

Childhood is a vital period to deliver obesity prevention strategies and possibly treatment strategies for those who are already obese with promising, clinically meaningful reduction in BMI Z score (Danielsson et al., 2012, Matson and Fallon, 2012, Baidal and Taveras, 2012). However, adolescent obesity treatment is also crucial to address in order to prevent an upcoming generation of obese adults with multiple comorbidities.

Paediatric obesity is a multifaceted public health problem which requires urget prevention and treatment strategies (Avis et al., 2014). Effective treatment strategies are probably population specific to some extent, and require a testing process to come up with the most successful, population specific treatment option (Reinehr and Wabitsch, 2011).

The original thesis plan, which aimed to explore the feasibility and efficacy of adolescent obesity family-based treatment intervention on BMI Z score, health related quality of life and cardiometabolic risk factors in Kuwait, started from Glasgow with the agreement of

the Higher Degree Committee of the University of Glasgow to conduct the treatment trial in Kuwait for a 12 month period (Glasgow PhD degrees permit a maximum of 12 months to be spent outside of Glasgow). The next stage started in Kuwait with the approval of the Medical Research Committee of the Ministry of Health to conduct the trial in Kuwait with the collection of baseline measurements that included anthropometric, health related quality of life assessment and blood samples, and the collection of end of trial measurements of the same parameters.

The original plan was cut short and the thesis plans were modified to describe an obese adolescent treatment intervention in Kuwait (NATTO treatment manual chapter 3), the results of the NATTO study in relation to primary outcome which was BMI Z score and secondary outcomes which were percentage body fat, blood pressure and waist circumference (chapter 6), health related quality of life of a sample of obese Kuwaiti adolescents compared to healthy weight peers and compared to their parent-proxy reports (chapter 4), and the prevalence of cardiometabolic risk factors in a sample of obese Kuwaiti adolescents (chapter 5).

The modification of the original plan was mostly due to the bureaucratic system in Kuwait which hindred the gathering of end of trial assessment of cardiometabolic risk factors and health related quality of life data, combined with the university limitation on the amount of time which could be spent outside of Kuwait. Our original ethical approval included baseline and end of trial assessment of primary outcome (BMI Z score) and secondary outcomes (percentage body fat, cardiometabolic risk factors and health related quality of life assessment). However, at the schools that agreed to participate in the study, school principals refused to allow the author assessment of participants heath related quality of life by means of Peds QL 4.0 questionnaire due to the schools' time restraints and only assessment of the participants weight, height and blood pressure was permitted at follow up. University of Glasgow PhD regulations, as noted above, meant that the author only had 12 months in Kuwait for the trial conduct and completion and starting a fresh process of ethical approval was out of the question. The author was faced also with refusal for end of trial blood samples collection. The head of laboratory department approval was needed to appoint the author a nurse and an equipped room. He specifically asked for a new ethical approval and a letter from the supervisor Professor John Reilly addressed to him directly to give permission to the author collecting end of trial blood samples. Sadly, the importance of the research was not on the agenda discussed with the school principals or the head of

the lab department and it didn't matter that the original ethical approval was valid. From all of the above, the author had to consider each study as separate namely; health related quality of life of obese adolescents in Kuwait (chapter 4) (Boodai and Reilly, 2013), prevalence of cardiometabolic risk factors and metabolic syndrome in obese Kuwaiti adolescents (chapter 5) (Boodai et al., 2014a) and National Adolescent Treatment Trial for Obesity in Kuwait (NATTO, chapter 6) (Boodai et al., 2014b).

This final chapter considers the main findings of the thesis studies, and highlights the implications of these findings in adolescent obesity treatment interventions in the future, with particular emphasis on Kuwait and the Gulf states. It also highlights the limitations of the thesis studies and future directions to minimise these limitations.

7.1 Reaffirmation of the main thesis findings

Chapter 6 in this thesis discussed the results of a family based obesity treatment RCT for Kuwaiti adolescents in terms of feasibility and some evidence of efficacy (Boodai et al., 2014b). The power calculations were based on the SCOTT trial (Hughes et al., 2008). Random school selection was not possible and only schools who agreed to participate were selected. Participants in the study were fairly homogenous in that all attended state schools and all were Kuwaiti nationals. The chapter concluded that performing RCT for the treatment of adolescent obesity in Kuwait is feasible. The feasibility was judged in terms of collecting baseline and end of trial measurements of primary and secondary outcomes. Efficacy of the treatment intervention was also tested and the chapter showed that the intervention had no effect on primary (BMI Z score) or secondary outcomes (percentage body fat, waist circumference, and blood pressure). The study was a wellconducted RCT, which followed the CONSORT guidelines (Moher et al., 2012), and in all areas of scientific research negative results should be of as much importance as positive ones. The intervention programme was intended to be reproducible, high intensity programme in comparison to typical dietitic care within the primary care system of Kuwait. Intensity of the sessions had to be reduced due to participants' incompliance. The health system in Kuwait is still lacking an integrated mutidisciplinary service for the treatment of paediatric obesity, in particular clinical psychologist services. Therefore the typical dietitic approach in treating paediatric obesity has no reference to behaviour modification techniques applied in the NATTO study. The need for more intensive and longer treatment programmes may well have the influence on the success of clinical management of paediatric obesity. In the most recent systematic review and meta-analysis of comprehensive behavioural

interventions for treating paediatric obesity, the authors concluded that using behavioural techniques in improving dietary habits, physical activity and sedentary behaviour could reach an overall average reduction of 0.47 in BMI Z score corresponding to a medium effect size (Janicke et al., 2014). The length of follow up in the selected studies ranged from 10 to 24 months, where improvement in weight outcomes were maintained provided that greater session intensity and treatment duration were present (Janicke et al., 2014). The degree of parents involvement had no effect on weight changes of their offspring, but their adherence to the behavioural techniques had great effect on their offspring's weight outcome (Janicke et al., 2014). During the conduct of the NATTO trial, the author had to decrease the intensity of the treatment intervention due to participants' lack of compliance as described in chapter 6. Moreover, it was not possible to collect follow up data beyond 6 months due to time restraints in Kuwait as the Higher Degree Committee in the University of Glasgow only allowed the author 12 months of research. Preparation, recruitment and baseline data collection started in September 2009, as mentioned in chapter 2. The start of the NATTO study was in January of 2010 and the last group session was in May 2010. The 2010 school year ended in June 2010, therefore end of trial measurements were carried out in June 2010. The mentioned timeline was very limiting to the research team and is one of the major limitations of the NATTO study.

An add on qualitative study is critical in assessing what the participants' likes and dislikes about the intervention and assessing their needs and support from outside the family with their suggestions for how the intervention could be improved in the future. The impact of cultural differences is very crucial, and interventions worked in one setting may not be as effective elsewhere. Therefore, part of the study design should also include pre-trial evaluation to let the participating subjects be part of the decision making of how to implement the intervention in question, within the evidence-base frame.

No measurement of in changes dietary intake/habits was undertaken. Such measurements may have given a valuable insight into the types of changes undertaken by the adolescents and their families. It was also unfortunate that data on physical and sedentary behaviours was not included in the results. Dietary habits and physical activity level would have been useful and which might have changed even in the absence of major changes in anthropometry.

Chapter 4 discussed the results of a comparison of health related quality of life between obese Kuwaiti adolescents and healthy weight peers and between obese Kuwaiti adolescents and their parents' perception of their health related quality of life (Boodai and

Reilly, 2013). The assessment tool for HRQL was the Peds QL 4.0 questionnaire (Varni et al., 2003). Decreased health related quality of life has been considered the norm in obese children and adolescents (Pulgaron, 2013, Ul-Haq et al., 2012, Al-Akour et al., 2012, Hamzaid et al., 2011, Griffiths et al., 2010, Riazi et al., 2010, Varni et al., 2007, Hughes et al., 2007), but in the study described in chapter 4 the HRQL of obese Kuwaiti participants did not differ much from that of the healthy weight peers except for the physical domain of the Peds QL 4.0 questionnaire (Boodai and Reilly, 2013). This result could contribute to the low attendance and compliance of participants at the NATTO study, pointing to their relatively undisrupted HRQL. This chapter gives an obvious message to researchers and health professionals that culture is an important factor in determining health effects of obesity, particularly mental health and well being, and international results from western countries might not be applicable in Kuwait.

Finally, chapter 5 was based on baseline measurements of cardiometabolic risk factors in 80 obese Kuwaiti adolescents participating in NATTO. The chapter also discussed the prevalence of metabolic syndrome using the IDF and the ATP III criteria (Zimmet et al., 2007, Panel, 2001). Seventy seven out of the 80 obese participants (96.3%) had at least one cardiometabolic risk factor. Almost a third of participants had MS. The chapter pointed out that if these results had been available for participants in the NATTO trial, attendance might had been better at the intervention sessions, assuming that concern over cardiometabolic risk factors could be used to motivate attendance. The chapter re-emphasises the importance of finding a treatment intervention for adolescent obesity, since multiple cardiometabolic risk factors increase the risk for later cardiometabolic disease.

7.2 Implications of thesis findings and future research suggestions

This thesis tried to explore the feasibility of conducting adolescent obesity treatment RCT in Kuwait. The literature still lacks any evidence of paediatric obesity treatment intervention trials from Kuwait and the Gulf region (Musaiger, 2012). Conducting an obesity treatment RCT in Kuwait was feasible as shown in the present study, but only with difficulty. Lack of resources, lack of support from the Kuwaiti authorities, lack of time in Kuwait, and lack of engagement with treatment all restricted our research plans. Our findings emphasise the urgent need for local paediatric obesity treatment approaches.

If we or other researchers attempt to conduct a ‘NATTO 2’ adolescent obesity treatment trial in the future, an alternative approach is required, a more ‘bottom-up’ approach

following the recommendations in the UK MRC statement on the development and evaluation of complex interventions, which was published only after the NATTO study was conceived in 2007/2008 (Craig et al., 2008). This would include a pilot study before the conduction of the RCT. An exploratory trial is indicated by the UK MRC Framework in order to check for the feasibility of the intervention tested within the context in which the intervention is being undertaken.A qualitative arm of the study which attempts to understand adolescent and parent perspectives, and to use this understanding to design a more acceptable, family tailored treatment protocol, and to identify the key barriers in changing their dietary and physical activity habits and in engaging more with the treatment (Craig et al., 2008). The fact that there was no statistically significant difference between the groups in reduction of BMI Z score would suggest that the intervention group still required to make further lifestyle changes. It is possible that in the intervention programme employed in the present study there were too many new concepts and strategies implemented compared to the standard treatment. The traffic light diet scheme was used and a variety of behavioural change techniques were employed. All of these were a substantial change from the typical dietetic care, therefore make comparison of differences complex.

More money, support and manpower will also be needed for future research of this kind- the data collection phase of the present study was supported by the resources of the author and a small bench fee to meet study running costs. Follow up in future treatment RCT should ideally be as long as possible and no less than 12 months from baseline. Another possible scenario is to conduct future 'NATTO 2' in schools rather than primary care clinics. Schools hold great promise in delivering treatment intervention with potential success (Almas et al., 2013, Sahota et al., 2001a), though in the present study some problems in dealing with schools in Kuwait have been noted.

Individual-level theories, community-level theories, interpersonal communication, printed materials, interactive computer technologies, and media campaigns these represent but a few of the tools available for the health professionals for designing, implementing, and evaluating health behavior change programs. Typically, a problem affecting a particular population has been identified, and the health professional must do something to fix the problem, whether it is high rates of obesity among children and adolescents in a community or inappropriate use of emergency departments for nonurgent care. If the NATTO study being done again, the use of the health programme planning which is a model for cost-benefit evaluation framework proposed by Green and Kreuter, would be

helpful in the study design. It involved the processes of health problem diagnosis, careful planning and continuous evaluation of the intervention proposed to hopefully create a successful intervention (Crosby and Noar, 2011, Green and Kreuter, 2005). At planning phase, researchers should expand their understanding of the community in which they are working by conducting multiple data collection activities that involve observations, surveys, focus groups with members of the community and concept mapping. Concept mapping is the term used to allow participants to generate a large number of ideas that are then subjected to quantitative analysis. Final agreement is reached on the concept maps that best reflect the participants' views. The second phase involves the essessment of the problem at hand using national datasets, which in Kuwait are readily available from the KNSS mentioned in chapter 1. This phase also involves the behavioural assessment at three key levels. The first one concerns the individual's behaviour contributing to the health problem, the second level concerns the behaviour of others who can directly affect the behaviour of the individual with the health problem, and the third level is the action of decision makers whose decisions affect the social or physical environment that influences the individuals with the health problem. After selecting the relevant behavioral and environmental factors for the intervention,selection of behavioural modification techniques should be in place to initiate the intervention designed. After implementing the intervention, a plan for data collection should be in place for process evaluation, and the intervention outcomes (Green and Kreuter, 2005).

The application of the health programme planning model and the UK MRC framework would have been more reliable in designing the NATTO trial, and helped in exploring the reasons behind lack of family engagement in the intervention , and participants suggestions for how the intervention could be improved in the future.

It is also possible that health care professionals lack the knowledge necessary to address paediatric obesity and treat it (Findholt et al., 2013), therefore, further research is needed to examine the foundations of the health care system involved in dealing with obese paediatric population in terms of assessment, internal nutrition knowledge, and management. Parents and health professionals need to be educated that childhood obesity is associated with medical comorbidities and is not simply a social or cosmetic concern (van Emmerik et al., 2012, Reilly and Kelly, 2011).

Currently, there is no clear assessment of behaviour modification techniques that are most effective in the treatment of paediatric obesity (Martin et al., 2013). Martin and colleagues(2013) assessed studies that have used behaviour change techniques to promote healthy eating and increase physical activity for paediatric obesity prevention and treatment. The effectiveness of interventions is probably being opposed by the inclusion of BCTs that are ineffective in achieving clinically meaningful reductions in BMI, and this may explain why such interventions fare so poorly in achieving (and maintaining) larger reductions in BMI over time. Potentially effective behaviour modification techniques were identified, however, more research is needed to identify targeted treatment interventions (Martin et al., 2013). Identifying the active components of interventions aiming to manage obesity in adolescents is very crucial and different from those used in the treatment of obesity in children. Possibly with 'NATTO 2', application of these potentially effective behaviour change techniques could result in better treatment outcomes.

The health related quality of life study in chapter 4 could be expanded in the future to involve more participants, with the involvement of private as well as public schools. Another future approach might be to use a disease-specific QoL instrument, rather than a generic instrument, since disease specific instruments might reveal small QoL deficits not revealed by generic instruments. For example, the Impact of Weight on Quality of Life (IWQOL-Kids) questionnaire is a new disease specific valid and reliable tool used to assess weight-related quality of life of obese adolescents (Modi and Zeller, 2011). In future, the IWQOL-Kids questionnaire could be translated to Arabic and used to assess weight related quality of life in obese Kuwaiti adolescents. It is designed to be used by adolescents, contains 27 items with each item begins with the phrase 'because of my weight ..', and is sensitive to differences between overweight and obese groups, and between clinical and community samples (Modi and Zeller, 2011).

For further research in the assessment cardiometabolic risk factors in obese Kuwaiti adolescents, it would be of great value if results be available at the preparatory stage of treatment RCT before group allocation, as these might provide a form of 'wake up call' for families participating in the trial. Attendance of both control and intervention groups could possibly be encouraged and retainability improved. Moreover, having baseline and end of trial assessment of cardiometabolic risk factors adds clinical value to the assessment of the efficacy of the tested intervention.

To sum up, we still have some way to go in understanding the environmental, cultural and other influences on the development of obesity in children and adolescents, and developing effective interventions that change obesity related behaviours. If we continue the preventive and treatment research in parallel, across the biological, behavioural and environmental disciplines, then we will make small changes, which taken together, will lead to social and societal change that will optimally result in a reversal of the obesity epidemic in the coming decades.

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Appendix A

WELCOME…….

Dear parents and children;

Firstly I would like to welcome you all into the first childhood obesity treatment trial to be conducted in Kuwait. It is also my pleasure to thank you for your valued participation in this trial that if proved to be a success, hopefully will be the first step into producing guidelines towards proper management of childhood obesity. If however the results are not encouraging; this will mark our next step into finding other useful tools to tackle childhood obesity in Kuwait.

Background:

Childhood and adolescence obesity in Kuwait is reaching escalating levels. It has detrimental effects on child's physical and psychological health. Unfortunately, there is no consensus on the most appropriate treatment method. Evidence is urgently needed to come up with population specific and effective treatment programmes. This study examines the effect of group therapy programme in treating obesity in a cohort of 10 to 14 year old adolescents. We will examine the effects of treatment on weight, body mass index, psychological health and cardiovascular disease risk factors.

Information about the study:

The research is conducted by Dr Shurooq Boodai, a Medical Registrar in Central Nutrition Clinic Food and Nutrition Administration, Ministry of Health. She is currently a PhD student at University of Glasgow, UK. The research is basically the pivot of her research degree and is taking place under supervision of Professor John Joseph Reilly-University of Glasgow.
As stated in the informed consent form, participation in this study is completely optional with no obligatory effects taking place at any point during the trial.
The trial outline has been reviewed and approved by the Ethical Committee for Medical Research-Ministry of Health-Kuwait.

Mapping the study:

After recruiting the appropriate number of adolescents into the study, a computer generated programme will divide the cohort into two groups; the intervention group who will receive the hypothesized group therapy, and the control group who will receive the welcome pack and will be given an appointment at the end of trial for end of trial assessment. There will be equal chance of enrollment into either group. At this point both groups and parents will be asked to answer a mini quality of life questionnaire.
Before group assignment, there will be given an appointment to attend the first one to one interview with the researcher. Here, a thorough medical history and examination will take place and blood samples will be collected. Weight and height will be measured and plotted on percentile charts.
The treatment sessions for the intervention group will take place thereafter in a lecture hall of Al Faiha'a polyclinic. They will be held every month for a period of 6 months. Each session will run for 60 minutes and another 15 minutes will be assigned for questions. Refreshments will be served at the end of each session.
At the sixth month all groups will be an end of trial reassessment of weight, height and another set of blood samples. Also, a mini quality of life questionnaire will be distributed.
Analysis of results and comparison of inter and intra group findings will take place in University of Glasgow.

السلام عليكم,

أنا د. شروق عبداللطيف بودي, أقوم حاليا بإجراء دراسة الدكتوراة حول استحداث طريقة مبتكرة لعلاج سمنة اليافعين (10 إلى 14 سنة). لقد قمنا بإجراء قياسات للطول والوزن لهؤلاء اليافعين عن طريق زيارات ميدانية لمدارسهم ومن ثم تصنيفهم على حسب كتلة الجسم إلى من يعانون من السمنة. ومن ثم سوف أقوم باستقبالهم للمرة الاولى في عيادة التغذية في مستشفى الصباح لأخذ التاريخ المرضي كاملا و فحصهم فحصا دقيقا وأخذ عينة دم لتحليلها في مختبر جلاسجو في اسكتلندا حيث أدرس. بعد ذلك سوف يتم تقسيم المجموعة إلى قسمان: قسم يدرج في جدول علاجنا وقسم سوف يقدم له ما هو متوفر حاليا لعلاج السمنة من عيادة التغذية, علما بأن التقسيم سوف يتم بشكل عشوائي باستخدام برنامج خاص. هذا ويتضمن العلاج تقسيم اليافعين إلى مجموعات صغيرة نجتمع بهم كل اسبوعين إلى شهر تقريبا على مدى 6 شهور وهي مدة البحث وذلك لتقديم برنامج العلاج الذي يحوي نصائح طبية و تغذوية علما بأن مكان الاجتماع هو مستوصف

الفيحاء في قاعة المحاضرات في الفترة المسائية. وبعد انتهاء كل جلسة سوف نقدم وجبة صحية خفيفة مع المشروبات. وفي نهاية البحث سوف نجري نفس الفحوصات التى قمنا بها في البداية. إن هذا البحث يعتبر الأول من نوعه بالنسبة لعلاج سمنة اليافعين في الكويت ويحمل أهمية كبيرة لمسيرة البحث العلمي بشكل عام لذا فمشاركتكم فيه تعتبر حيوية جدا ولكنها غير ملزمة, وعليه فإن لكم مطلق الحرية للانسحاب من البحث في أي مرحلة من مراحله دون أي التزام وأود أن أنوه بأن البحث لن يؤثر سلبا على الطلبة صحيا أو دراسيا.
إذا وافقتم على الاشتراك أرجو التكرم بالتوقيع على الاقرار المستنير وبعدها سأوافيكم بمواعيد العيادة الصباحية خلال شهر ديسمبر

The National Adolescence Treatment Trial for Obesity

NATTO 2009-2010

إقرار مستنير
Informed consent

أقر أنا ..... بصفتي ..... الطفل ..... البالغ من العمر ..... سنة بأن الباحثة د. شروق عبداللطيف بودي التي تقوم بعمل رسالة الدكتوراة تحت عنوان علاج سمنة الأطفال في الكويت قد شرحت لي أن الهدف من البحث هو وضع برنامج لعلاج السمنة بين الأطفال وأن طريقة البحث تتضمن الحصول على معلومات حول الطفل من ملفه بالمدرسة ثم إجراء قياسات بدنية للوزن والطول ومحيط الخصر وتقدير كتلة الجسم BMI SD score وفي حالة اكتشاف أن الطفل مصاب بالسمنة (BMI >95th centile) فإنه سيتم تحويله إلى عيادة التغذية بإدارة التغذية والإطعام بمستشفى الصباح لإجراء القياسات البدنية وأخذ عينة دم(5ml) من الطفل وبعدها سيدرج الطفل إما في قائمة البرنامج الغذائي intervention group(أي سيتم إعطاؤه النصائح التغذوية) أو في قائمة المجموعة الضابطة control group(أي لن يستلم النصائح التغذوية) حيث سيتم الإدراج بشكل عشوائي بدون أفضلية. أما في نهاية فترة الدراسة بعد 6 شهور فإنه سيتم استدعاء الطفل مرة ثانية و أخذ القياسات السابق ذكرها و أخذ عينة دم أخرى (5ml) علما بأن عينات الدم سيتم إرسالها إلى الخارج لتحليلها في جامعة جلاسجو للتعرف على فعالية البرنامج ولن تجرى عليها أي فحوصات أخرى غير تلك المحددة ببروتوكول الدراسة. وأن الاشتراك في الدراسة اختياري وليس إجباري ولن يترتب على الرفض أي أضرار على الطفل كما أن المشاركة بالدراسة لا يترتب عليها أي أضرار على الطفل في أي مرحلة من مراحلها. كما أقر أنني على علم أنه سيتم تداول المعلومات المزودة بسرية تامة حفاظا على مصلحة الطفل وشرف المهنة.

في حالة الموافقة:

وقد وافقت بكامل إرادتي ودون أي ضغط على أو على طفلي مشاركة .....في هذه الدراسة وهذا إقرار بذلك علما بأن الباحثة قد أوضحت لي أن من حقي الانسحاب من الدراسة في أي مرحلة دون أن يترتب على ذلك أي أضرار علما بأن الطفل موافق ولم يتعرض لأي ضغوط للمشاركة في هذه الدراسة.

الاسم: .....

التوقيع: .....

التلفون: .....

الصلة بالطفل: .....

هل يعاني طفلك من أي مشاكل صحية غير السمنة؟ .....

من ماذا؟ .....

اسم الباحثة: .....

في حالة عدم الموافقة:

أقر بأنني لا أوافق على الاشتراك في الدراسة .

الاسم: .....

التوقيع: .....

التلفون: .....

الصلة بالطفل: .....

اسم الباحثة: .....

Ethical Approval

6.

STATE OF KUWAIT
MINISTRY OF HEALTH

دولـة الكـويت
وزارة الصحـــة

Reference WSA/112
Date 12/2/09

الرقم : ١١٢/ع ص
التاريخ : ١٢/٢/٢٠٠٩

السيد الفاضل/ وكيـــل الـــــوزارة المحترم
تحية طيبة وبعد،،،

الموضوع: تسهيل مهمة الباحثة

د٠ شروق عبداللطيف محمد بودي
مبعوثة الدكتوراه بكلية الطب جامعة جلاسجو

يرجى الإحاطة بأن اللجنة الدائمة لتنسيق البحوث الطبية والصحية قد ناقشت باجتماعها الرابع (٢٠٠٩/٤) المنعقد بتاريخ الأحد ٢٠٠٩/٢/١ بروتوكول البحث المقدم من د٠ شروق عبداللطيف محمد بودي مبعوثة الدكتوراه بكلية الطب/ جامعة جلاسجو تحت عنوان:

Kuwait Childhood Obesity Treatment Trial

(دراسة حول طريقة علاج سمنة الأطفال في الكويت للمرحلة العمرية ١٠-١٤ سنة)٠
ويتم البحث بعيادات التغذية بإدارة التغذية والإطعام عن طريق استخلاص بعض البيانات عن الأطفال المشمولين بالدراسة من ملفاتهم بالمدرسة وإجراء قياسات بدنية للـوزن وللطـول ومحيط الخصر وتقدير كتلة الجسم BMI والحصول على بعض البيانات من أولياء الأمـور عن طريق الاستبيان ٠
(النسخة العربية من استبيان (Peds QI) وأخذ عينة دم (5ml) من بعض المشمولين بالدراسة وأخذ عينة أخرى 5ml بعد ٦ شهور بعيادات التغذية (العينة المستهدفة بالدراسة ٢٠٠ طفل) ويتضمن البحث إرسال عينات الدم إلى جامعة جلاسـجو/ بالمملكـة المتحـدة لإجراء الفحوص المخبرية المطلوبة ٠

Cables : HEALTH KUWAIT
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برقيا : صحـة الكـويت
الوزارة المالية المستودعات
ص.ب : ٥ ١٥١٩ ٢٢٥٧٥
الرمز البريدي للوزارة ١٣٠٠١

7540 HA 0009622

Reference ..... الـرقـم : .....

Date ..... التـاريخ : .....

وقد أوصت اللجنة بالموافقة على إجراء البحث مع إلتزام الباحثة بالمحافظة على سرية المعلومات وعدم تداولها خارج إطار البحث والحصول على الموافقة الحرة المستنيرة المسبقة Informed Consent من الولي القانوني لكل طفل من الأطفال المشاركين بالدراسة كما يتضمن الإقرار موافقة الطفل وكذلك الموافقة على أخذ عينتين من الدم (5ml لكل عينة) والموافقة على إرسال العينات للخارج مع تعهد الباحثة بعدم إجراء أي تحاليل إضافية خلاف التحاليل المحددة ببروتوكول الدراسة وإعداد إقرار مستقل للمجموعة الضابطة Control group (وقد تعهدت الباحثة أمام اللجنة بالاجتماع بالالتزام بذلك).

ونظراً لكون البحث يتم بعيادات التغذية بإدارة التغذية والإطعام وبموافقة السيدة مديرة إدارة التغذية والاطعام كما يتضمن إرسال عينات الدم لخارج البلاد لإجراء الفحوص المخبرية بجامعة جلاسجو.

يرجى بعد الإطلاع الموافقة على مخاطبة السيد/ الوكيل المساعد لشئون الخدمات الطبية المساندة لتسهيل مهمة الباحثة (مع مراعاة التنسيق المسبق مع إدارة خدمات المختبرات الطبية قبل إرسال عينات الدم خارج البلاد) وفقاً للضوابط الموضوعة لذلك والاجراءات المتبعة بهذا الشأن مع عدم تحمل الوزارة لأي تكاليف إضافية.

وتفضلوا بقبول فائق الاحترام،،،

رئيس اللجنة الدائمة

لتنسيق البحوث الطبية والصحية

الدكتور علي يوسف السيف

وكيل الوزارة المساعد

لشئون الصحة العامة

Cables : HEALTH KUWAIT

	Admin.	Financial Affairs	Medical Stores
P.O. Box :	5	1519	22575

E-Mail : health @ moh. gov. kw

Zip Code : 13001

برقيا : صحة الكويت

	الوزارة	المالية	المستودعات
ص.ب :	٥	١٥١٩	٢٢٥٧٥

الرمز البريدي للوزارة ١٣٠٠١

7540 HA 0009622

State of Kuwait
Ministry of Health

Date : 12.2.2009
Ref. : MPH/112
Mr. Under Secretary

Subject : Helping the researcher : Dr. Shurooq Abdullateef Boodai
PhD. Scholarship from Faculty of Medicine – University of Glasgow

This is to inform you that the Permanent Committee for Coordination of the Medical & Health Researches has discussed in its fourth meeting (4/2009) on Sunday 1.2.2009 the Research Protocol submitted by Dr Shurooq Abdullateef Mohammad Boodai , PhD Scholar from Faculty of Medicine / University of Glasgow under the title :

Kuwait Childhood Obesity Treatment Trial

The Research will be conducted at the Nutrition Clinics, Food and Nutrition Administration, through extracting the details about the children covered in the study from their school files, perform physical examination for weight, height and waist circumference, in addition to BMI, and some details to be taken from the Parents.

The Arabic version of the (Peds QL) and blood sample (5 ml) from the children covered by the study in addition to another sample (5 ml) after 6 months at the Nutrition Clinics (the targeted sample 200 children) . The research includes sending the blood samples to University of Glasgow / UK for performing the required Lab. tests.

The Committee recommends the agreement on the research but the researcher should preserve full secrecy of the details of the targeted sample and not to disclose any information out of the research scope and should obtain the informed consent from the parent of each child covered

BASSAM A. AZIZ
Certified Translator

by the study. The declaration also includes the agreement of the child, and the agreement to take two blood samples (5 ml for each sample) and the sending of the samples abroad.

The Researcher should promise not to perform any other additional lab tests, other than those of the study, and to prepare a separate informed consent for the Control Group. (The researcher promised to observe the above obligations before the Committee).

And as the research is conducted at the Nutrition Clinics, with the approval of the Head of Food & Nutrition Department, it also includes sending the blood samples abraod for lab tests at University of Glasgow.

Kindly, consider the above and approve the addressing of the Assistant Under Secretary for Allied Medical Services to facilitate the task of the researcher (observing the previous coordination with the department of Medical Labs before sending the blood samples abraod) according to the prescribed conditions and procedures. The Ministry in this respect shall not bear any additional Costs.

Best regards

(Signed)
D. Ali Yousef AL-Seif
Assistant Under secretary of Public Health
Head of the Permanent Committee of Medical Researches

The National Adolescence Treatment Trial for Obesity-Kuwait
(NATTO)
University of Glasgow
2009-2010
Anthropometry
Quality of life questtionnaire

الاسم:.....

تاريخ الميلاد:.....

المدرسة:.....

الصف:.....

الهاتف: المنزل:.....
الأم/ الأب:.....

الوزن(كجم):.....

الطول(سم):.....

كتلة الجسم (كجم/م^2):.....

الحالة: .....

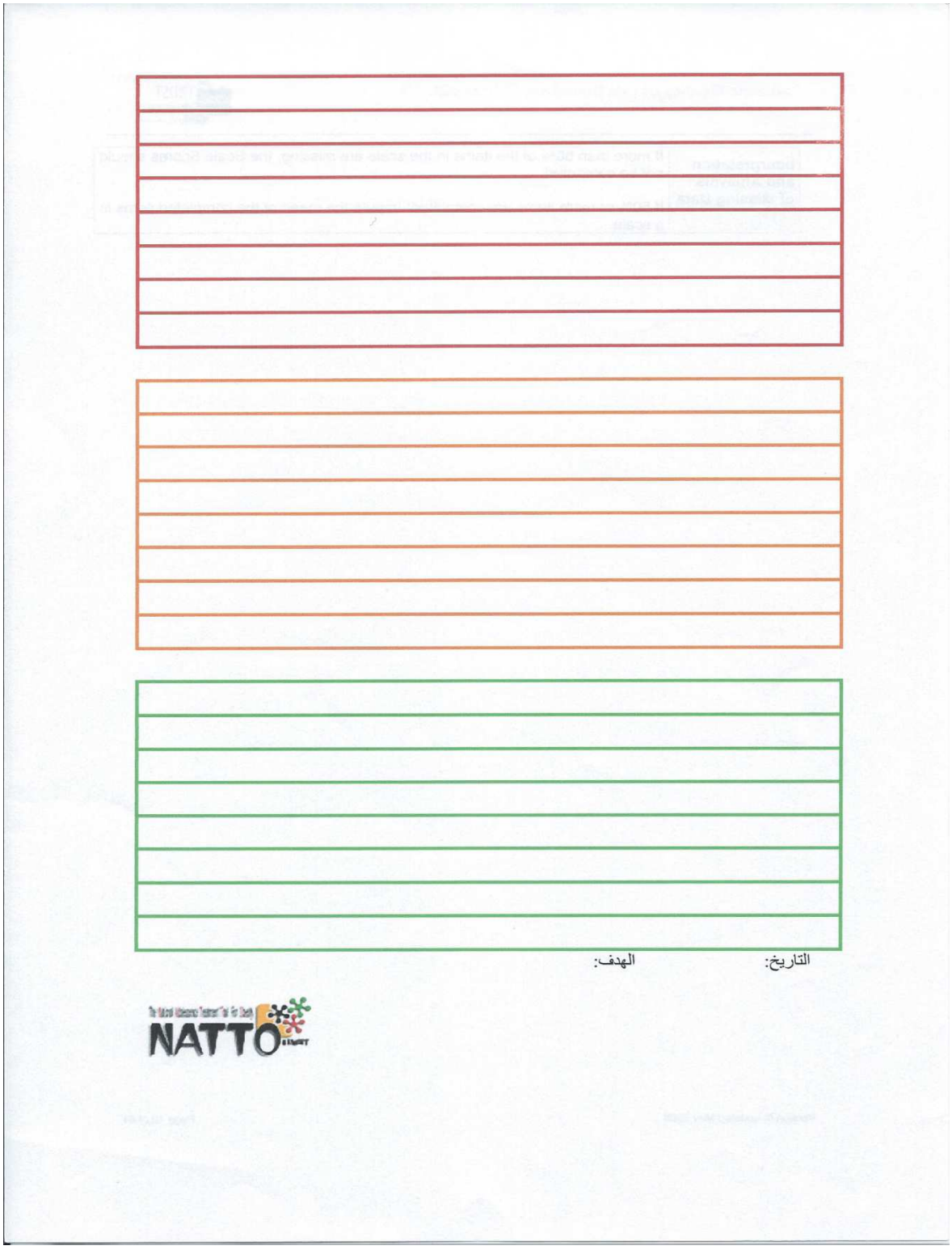
Quality of life questionnaire

الابن/ الابنة: ☐ **كامل** ☐ **غير كامل**

الأب/ الأم: ☐ **كامل** ☐ **غير كامل**

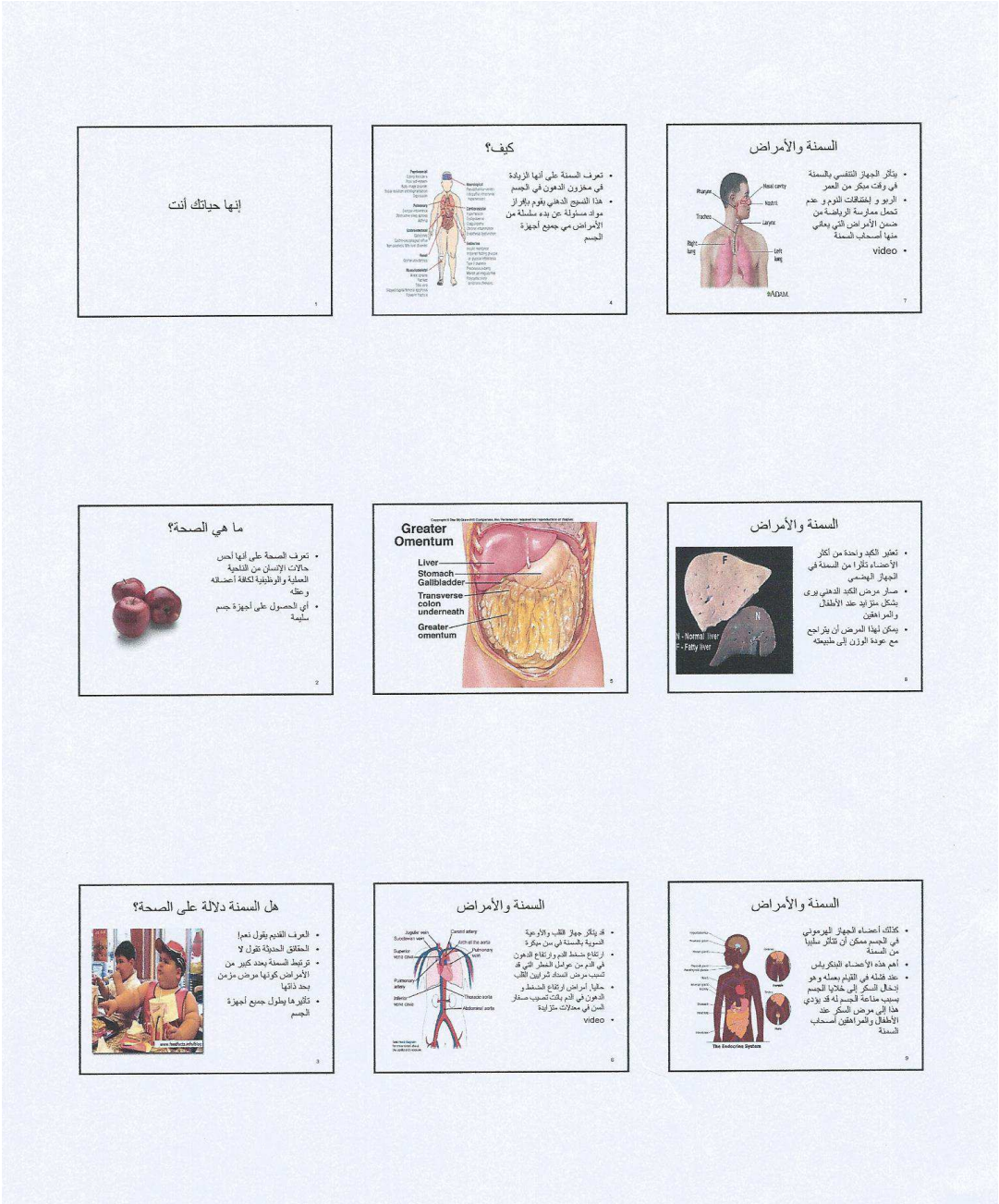
رقم التعريف:.....

My Log Book



The Treatment sessions aiding material

Session One

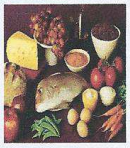


إبدأ

- ابقى مدونة بما تأكله وتفعله
- شارك الأهل في هذا الموضوع واعمل مع الجماعة
- حافظ على الاتفاق
- وليكن هدفك خطة عودة متفق عليها

16

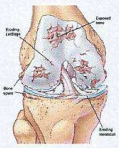
الغذاء



- يوفر الغذاء الطاقة والفيتامينات والأملاح والألياف التي يحتاجها الجسم
- الغذاء العالي بالسعرات الحرارية قد يسبب السمنة إذا أكثرنا من تناوله
- الغذاء العالي بالألياف الغذائية كذلك التي في الخضروات والفواكه والبقول تسبب الإحساس بالشبع لمدة أطول
- كما أن الخضروات والفواكه غنية بالفيتامينات والأملاح المهمة للجسم

13

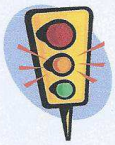
السمنة والأمراض



- يعتقد أنه بسبب زيادة الوزن و الحمل الثقيل على جهاز العظام والعضلات فإن أكثر الأعضاء تأثرا هي المفاصل والعظام في الجسم
- هنا تظهر الخشونة في سن مبكر جدا عما هو معهود

10

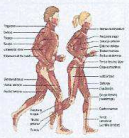
برنامج غذاء إشارة المرور



- هذا البرنامج سهل ويلخص الغذاء إلى ثلاث مجموعات
- أحمر للتوقف
- أصفر للحذر
- أخضر للاستمرار

17

النشاط الرياضي



- الجهاز العظمي العضلي يساعدنا على الحركة والتنفس
- وهو يحتاج إلى الطاقة ليقوم بمهامه على أكمل وجه
- ولأن العضلات تستهلك طاقة لكي تعمل فإنه كلما تحركت أكثر كلما استهلكت طاقة أكثر
- أما في حالة الخمول والكسل فإن الطاقة المستهلكة في أدنى مستوياتها

14

معادلة توازن الطاقة

- في حالة الاتزان وثبات الوزن فإن الطاقة الداخلة في الجسم من الطعام والشراب تساوي الطاقة المستخدمة من الجسم للحياة وهضم الطعام والحركة
- في حالة زيادة الوزن والسمنة فإن الجسم يستخدم طاقة أقل من التي يزودها الطعام والشراب الداخل إليه

11

الأحمر

- إنه الغذاء العالي بالسعرات الحرارية والمنخفض القيمة الغذائية
- يجب أن تقلل تناول هذا الغذاء
- الهدف أن تحد من تناول هذا الطعام إلى مرة واحدة في الأسبوع
- ابدأ عن طريق تناول كميات أقل أو في أيام متباعدة

18

كيف أبدأ؟

- قلنبدأ عن طريق وضع أهداف صغيرة وفي المتناول
- حافظ على بلوغ هذه الأهداف خلال الزمن الذي تتفق عليه مع الأهل
- لنبدأ العمل الجماعي لكي نصل لهذا الهدف
- وفي النهاية فلنتفق على جائزة مناسبة!

15

كيف وصلت إلى هذا الوزن؟

- إن ما تأكله من طعام عالي السعرات الحرارية يؤثر على نصف المعادلة
- النصف الاخر يتعلق بقلة الحركة والخمول
- هذان هما العاملان الرئيسيان لحدوث السمنة وتطورها

12

المناقشة

19

الأصفر





- يوفر هذا النوع من الغذاء الطاقة والبروتين
- زيادة تناول هذا الطعام عن الحد المطلوب يسبب زيادة الوزن
- حد من تناول هذا الطعام إلى الوجبات الثلاث
- وليكن الهدف الذهني هو تقليل الكمية المتناولة في هذه الوجبات

20

الأخضر

- هذا يتضمن جميع الخضروات والفواكه متعددة الألوان
- لك مطلق الحرية لتناول الكمية التي تريدها
- تناولها كبدائل للغذاء الأحمر
- ميزة هذه المجموعة أنها قليلة السعرات الحرارية وعالية القيمة الغذائية

21

كيف لي أن أصبح أكثر نشاطا؟




- اللعب ... في المدرسة أو المنزل
- قلل الوقت الذي تمضيه أمام الشاشة
- الهدف الذهني هو تمضية مدة لا تزيد عن ساعتين في اليوم أمام الشاشة
- ابدأ تدريجيا
- ولا تنسى أن أي نشاط تستخدم فيه عضلاتك يستهلك طاقة
- مثال: تراتيب السرير!

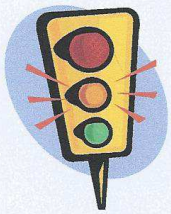
22

Session Two

استمتع بالحياة

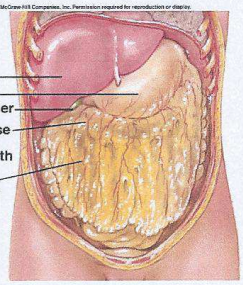
1

برنامج غذاء إشارة المرور



- هذا البرنامج سهل ويلخص الغذاء إلى ثلاث مجموعات
- أحمر للتوقف
- أصفر للانتباه
- أخضر للاستمرار

4



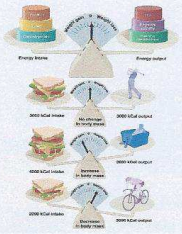
2

كيف لي أن أصبح أكثر نشاطا؟

- العب..... في المدرسة أو المنزل
- قلل الوقت الذي تمضيه أمام الشاشة
- الهدف النهائي هو تمضية مدة لا تزيد عن ساعتين في اليوم أمام الشاشة
- ابدأ تدريجيا
- ولا تنسى أن أي نشاط تستخدم فيه عضلاتك يستهلك طاقة
- مثال: ترتيب السرير!

5

معادلة توازن الطاقة



- في حالة الاتزان وثبات الوزن فإن الطاقة الداخلة في الجسم من الطعام والشراب تساوي الطاقة المستخدمة من الجسم للحياة وهضم الطعام والحركة
- في حالة زيادة الوزن والسمنة فإن الجسم يستخدم طاقة أقل من التي يزودها الطعام والشراب الداخل إليه

3

ما الذي حدث؟

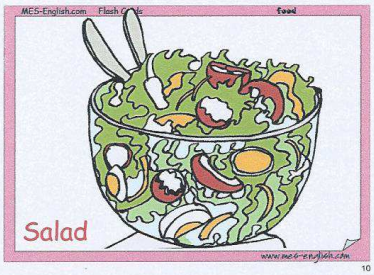
- تحديد الأهداف
- مراقبة النشاط ووقت الشاشة
- مراقبة كل ما يدخل داخل فمي
- الجائزة
- تعديل الأهداف
- المتابعة

6

تعرف على نمط حياتك

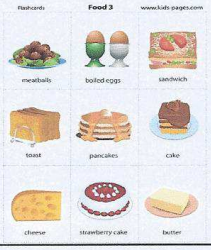
- ماذا تفعل عندما تستيقظ من النوم إلى أن تنام ؟
- هل تعي كل ما تفعل؟
- بعض الأمور تصبح عادة دون أن نشعر
- راقب ما تتناوله
- راقب ما تفعله

7



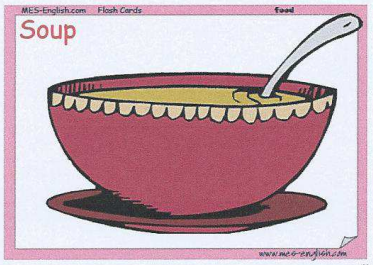
10

في الصباح



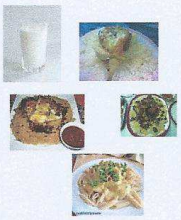
- ما هي أهمية الإفطار؟
- ماذا يجب أن يحتوي؟
- ماذا تأكل في المدرسة؟
- ما الذي يجعلك تختار هذه الوجبات؟
- هل تصنفها على أساس علمك ببرنامج إشارة المرور؟

8



11

الغذاء



- أين تأكل؟
- متى؟
- ماذا؟

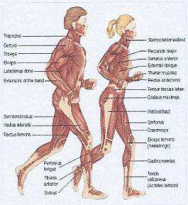
9

فترة العصر

- كيف تقضيها؟
- كم من الوقت تقضيه أمام الشاشة؟

12

النشاط الرياضي



- الجهاز العظمي العضلي يساعدنا على الحركة والتنفس
- وهو يحتاج إلى الطاقة ليقوم بمهامه على أكمل وجه
- ولأن العضلات تستهلك طاقة لكي تعمل فإنه كلما تحركت أكثر كلما استهلكت طاقة أكثر
- أما في حالة الخمول والكسل فإن الطاقة المستهلكة في أدنى مستوياتها

13

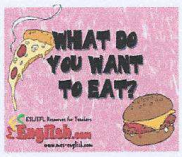
جدد الأهداف

- ضع من هدف إلى 3 أهداف جدد
- راقب نفسك طول اليوم وراقب ما حولك ... ما الذي يدفعك لفعل الأحمر ؟؟؟؟
- راقب وزنك وما حولك وحاول تغيير الأشياء لتتناسب مع خططك الجديدة
- للأهل..... قدم الدعم لكل تصرف إيجابي

16

العشاء

- هل هناك وقت محدد للعشاء؟
- هل تأكل لوحدك؟
- ماذا تأكل عادة؟



14

ما العمل؟

- وجبة الفطور هي أهم وجبة في اليوم
- تناول وجباتك مع العائلة
- تذكر نظام إشارة المرور
- تذكر أن تتحرك
- المشروبات الغازية والوجبات السريعة من المجموعة الحمراء
- ابحث عن البديل
- ولا تتسوق وأنت جائع

15

Session Three

كيف أختار غذائي

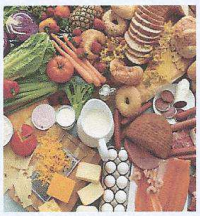
1

ماذا يوجد في القسم الأحمر؟

- السكر
- الدهون
- الملح
- قليييييييييييل بالقيمة الغذائية

4

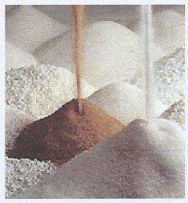
ماذا يوجد في الطعام؟



- يتركب الغذاء من مواد أولية تشكل حجمه وشكله وطعمه و ملمسه
- هذه المواد منها البروتينات والكربوهيدرات والدهون
- كما تمثل الفيتامينات والمعادن جزء بسيط من الغذاء
- ولا ننسى أن هناك مواد أخرى كالملوثات والألوان و غيرها

2

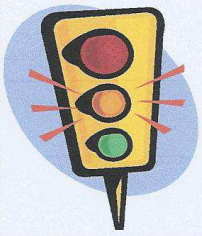
السكر



- يوفر أسرع مصدر للطاقة
- كلما حصلنا عليه من مصادر طبيعية (كالفاكهة) كلما قل الضغط على عمل البنكرياس
- ولكن عندما يزيد استهلاكنا للسكر بالتالي يفقد البنكرياس السيطرة و تبدأ أعراض مرض السكر بالظهور
- كما أن السكر يتحول إلى دهون يتم تخزينها في الجسم والدم

5

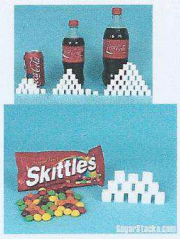
إشارة المرور



- قمنا بتقسيم الغذاء إلى 3 أقسام أخرى
  - الأحمر
  - الأصفر
  - الأخضر
- القسم الأحمر هو الذي يسبب الأمراض العصرية مثل.....
- يمكن تناوله مرة واحدة في اليوم وهذا هو الهدف

3

السكر



- ما مقدار السكر في الغذاء؟
- ومثلا كتكات 4 أصابع يحتوي على 15.5 ملعقة طعام سكر
- ويحتوي الآيس كريم على 10.5 ملعقة طعام سكر
- الدونت تحتوي على 12 ملعقة طعام سكر

6

الدهون

- مصدر مهم للطاقة والفيتامينات التي تذوب في الدهون
- يمكن الحصول عليه من قسم من اللحوم والسمك و المكسرات
- كما نحصل عليه من الأطعمة المقلية أو المعجنات
- زيادة الدهون في غذائنا سبب رئيسي للسمنة وتصلب الشرايين وأمراض البشرة

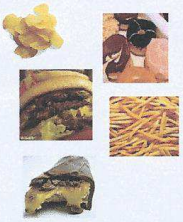
7

الملح

- يحتاج الجسم إلى 6جم من الملح يوميا (ملعقة أكل)
- لا يوجد حتى الآن مصادر عن معدل استهلاكنا للملح في الكويت
- لكن من قراءات الضغط يتضح لنا أننا نفوق المعدل
- وجبة واحدة من الوجبات السريعة توفر ما يقارب من ال 13 جم من الملح

10

الدهون



- يحتوي كيس الكرسبس على 2.5 ملعقة كبيرة من الدهون
- الدونت تحتوي على 5.5 ملاعق أكل من الدهون
- البيج ماك تحتوي على 6 ملاعق أكل دهون
- الفرنش فريز يحتوي على 2 أو 4 أو 8 ملاعق أكل دهون
- الكاكاو يحتوي على 5 ملاعق دهون

8

بالمقابل...

- التفاحة تحتوي على 2.5 ملعقة أكل سكر ولا تحتوي على دهون أو أملاح
- السكر المتواجد في التفاح من النوع البسيط سهل الهضم وبسبب وجود الألياف فإن مستواه يرتفع في الدم بشكل تدريجي
- هذا يعود على أغلب أنواع الفاكهة

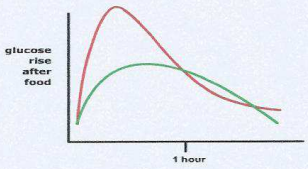
11

الملح

- يتكون من ذرات الصوديوم والكلور
- يضيف إلى الطعام نكهة مالحة نفضلها جميعا
- زيادته تسبب ارتفاع ضغط الدم عن طريق تضييق شرايين الكلى
- كما يسبب احتباس الماء في الجسم

9

هضم السكريات

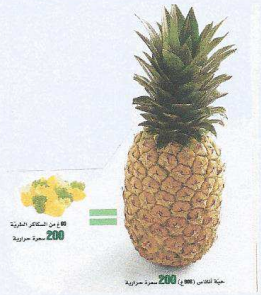


12

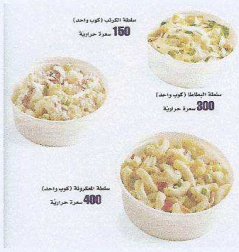
ماذا عن السعرات الحرارية؟

- ما هي؟
- كمية الطاقة الموجودة في الغذاء
- بعض الأغذية تكون عالية بسعراتها الحرارية ولكن قليلة بكميتها و قيمتها الغذائية
- يجب علينا أن نعي ما نأكل حتى لا تتكدس هذه السعرات على شكل دهون

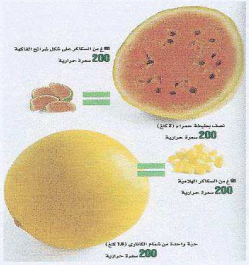
13



16



14



17

15

هل تعلم ما يحويه غذاؤك؟

Nutrition Facts

Serving Size ½ cup (114g)
Servings Per Container 4

Amount Per Serving

Calories 90	Calories from Fat 30
	% Daily Value
Total Fat 3g	**5%**
Saturated Fat 0g	**0%**
Cholesterol 0mg	**0%**
Sodium 300mg	**13%**
Total Carbohydrate 13g	**4%**
Dietary Fiber 3g	**12%**
Sugars 3g	
Protein 3g	

Vitamin A 80% • Vitamin C 60%
Calcium 4% • Iron 4%

*Percent Daily Values are based on a 2,000 calorie diet. Your daily values may be higher or lower depending on your calorie needs:

	Calories	2,000	2,500
Total Fat	Less than	65g	80g
Sat Fat	Less than	20g	25g
Cholesterol	Less than	300mg	300mg
Sodium	Less than	2,400mg	2,400mg
Total Carbohydrate		300g	375g
Dietary Fiber		25g	30g

Calories per gram:
Fat 9 • Carbohydrate 4 • Protein 4

- على كل علبة أو كيس هناك ركن خاص لتقديم المعلومات عن المنتج
- يجب علينا قراءة هذه المعلومات لنعرف كم سعرة حرارية, دهون, ملح, كربوهيدرات, بروتين, فيتامينات وأملاح

18

Session Four

تمتع بالصيف!

1

لا ننسى

- الأحمر يتضمن...
- هل تقرأ المعلومات الغذائية على الطعام

4

تذكروا

- ما نقوم به من أعمال يؤثر علينا أولا بشكل مباشر حتى لو لم نر النتائج فوريا
- أغلب الأمراض مثل الضغط والسكر وانسداد الشرايين تبدأ بدون أي مقدمات وتستمر في التطور إلى أن تظهر الأعراض في سن مبكر
- علينا الاعتراف أن بعض عاداتنا الغذائية تضرنا وعن قصد منا
- يجب أن نغير سلوكنا حتى نتمتع بالصحة والنشاط

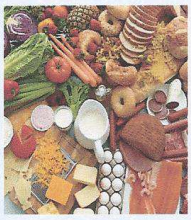
2

الأهداف

- من استلم الجائزة؟
- ما هي الأهداف القادمة؟

5

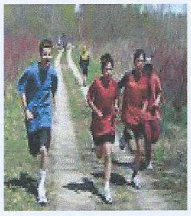
يوم مثالي ....



- الإفطار....
- المدرسة...
- الغداء...
- فترة بعد الظهر...
- العشاء....

3

معادلة الطاقة



- الحركة جزء مهم من معادلة الطاقة
- الرياضة يجب أن تشكل جزء أساسي من الروتين اليومي لنا
- مدة لا تقل عن ساعة يوميا كاملة أو بشكل متقطع
- هذا يتضمن المشي أو القفز أو الركض أو ركوب الدراجة أو رياضة الكرة بأنواعها والرقص

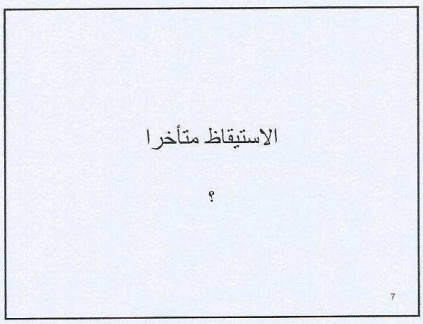
6

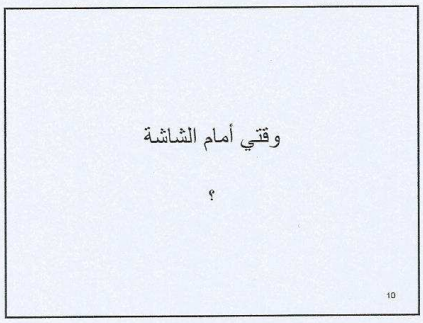
This session included rope jumping, and hula hoop exercise.

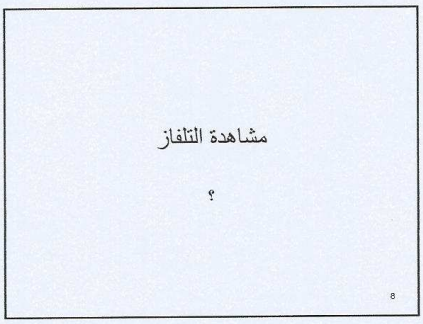
Session Five

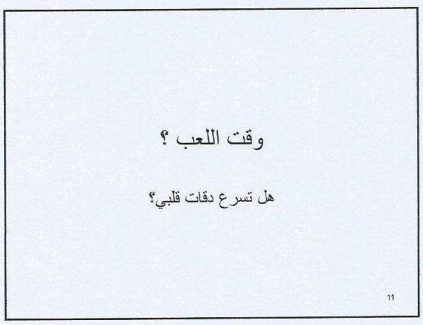
This session was a practical involving healthy snack making.

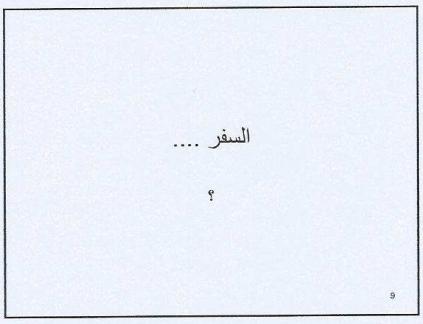
Session Six

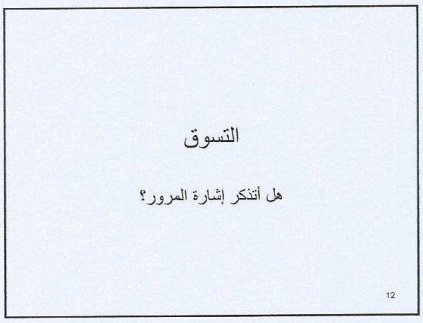

الاستيقاظ متأخرا
؟
7


وقتي أمام الشاشة
؟
10


مشاهدة التلفاز
؟
8


وقت اللعب ؟
هل تسرع دقات قلبي؟
11


السفر ....
؟
9


التسوق
هل أتذكر إشارة المرور؟
12

أين الأهل؟

الأم والأب ما رأيكم؟

13

هل شكلي يحسسني بالإحباط؟

هل بإمكاني التغيير؟
هل التغيير يحتاج إلى وقت؟
إذا لم أتغير هل سأصاب بأمراض؟

16

هل حققنا أهداف؟

هل نخطط لأهداف في المستقبل؟

14

ما فائدة الرياضة والغذاء الصحي؟

القلب
الكبد
الكلى
البلكريلس
الحالتي النفسية
الوزن

17

كم مرة أراقب وزني؟

هل أراقب ما آكل؟
هل أراقب ما أشرب؟
هل أراقب حركاتي ووقتي؟
مثال....

15

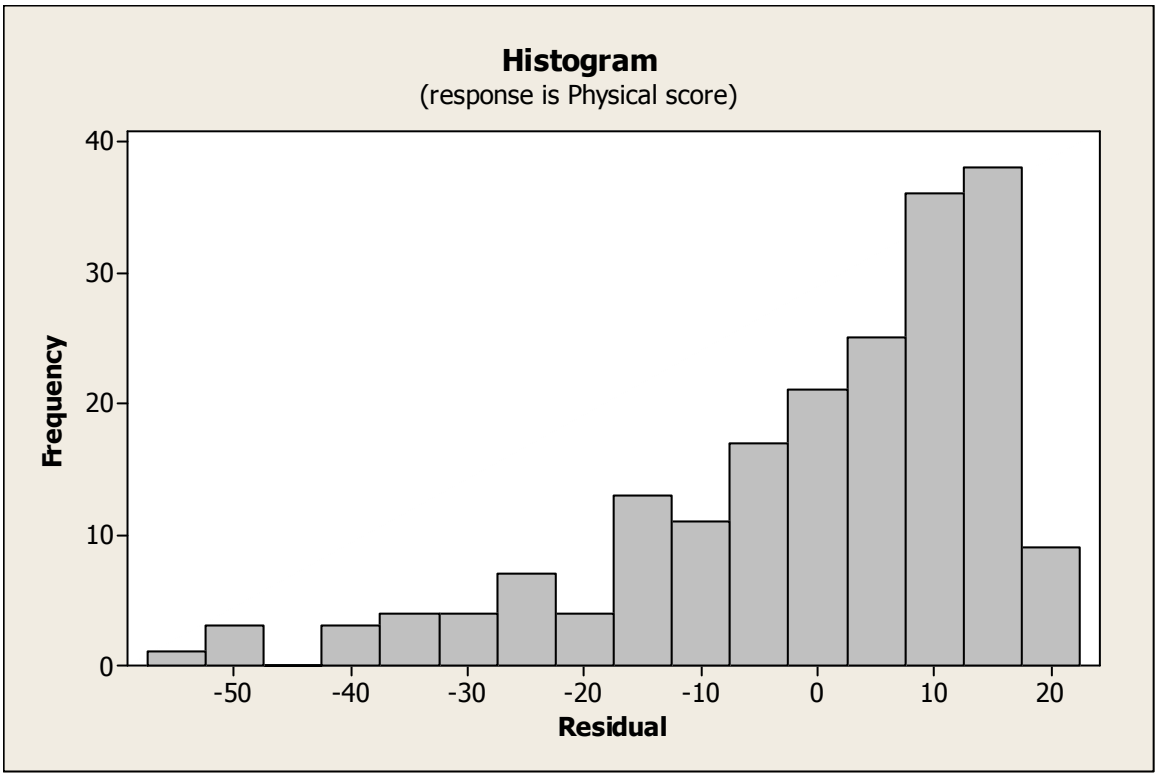
رحلتي في الصيف هدفها

أنا

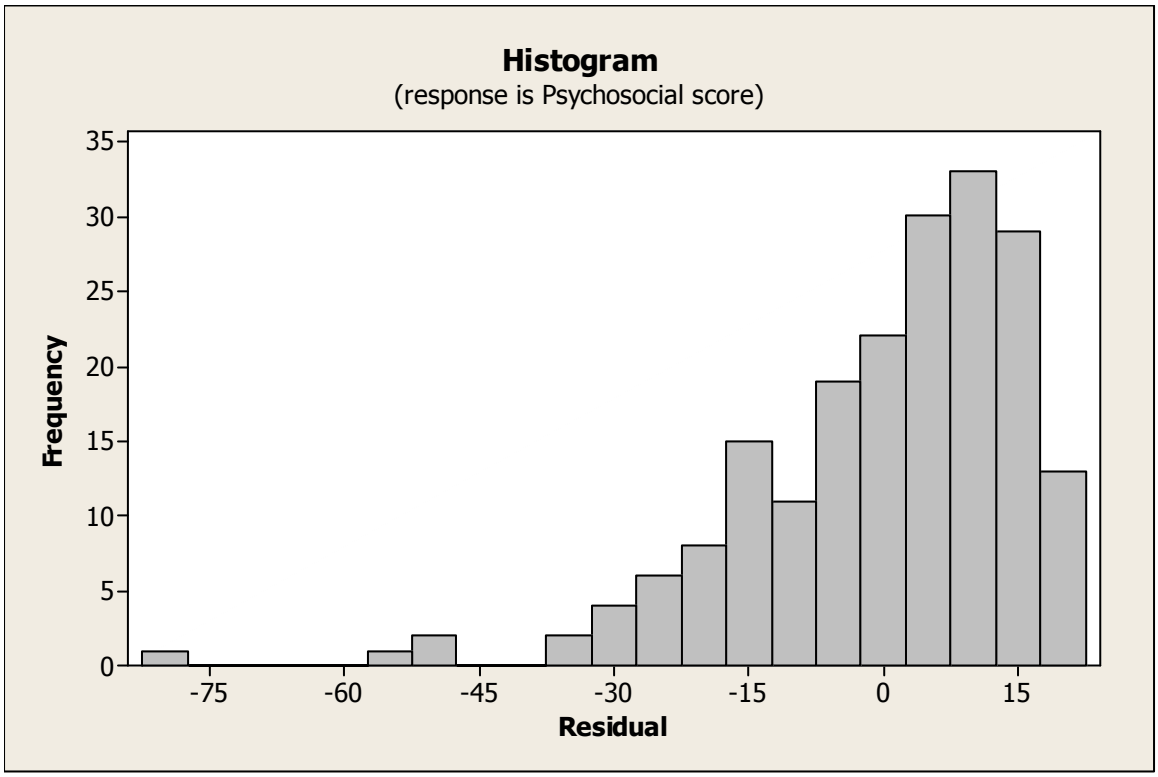
18

Appendix B

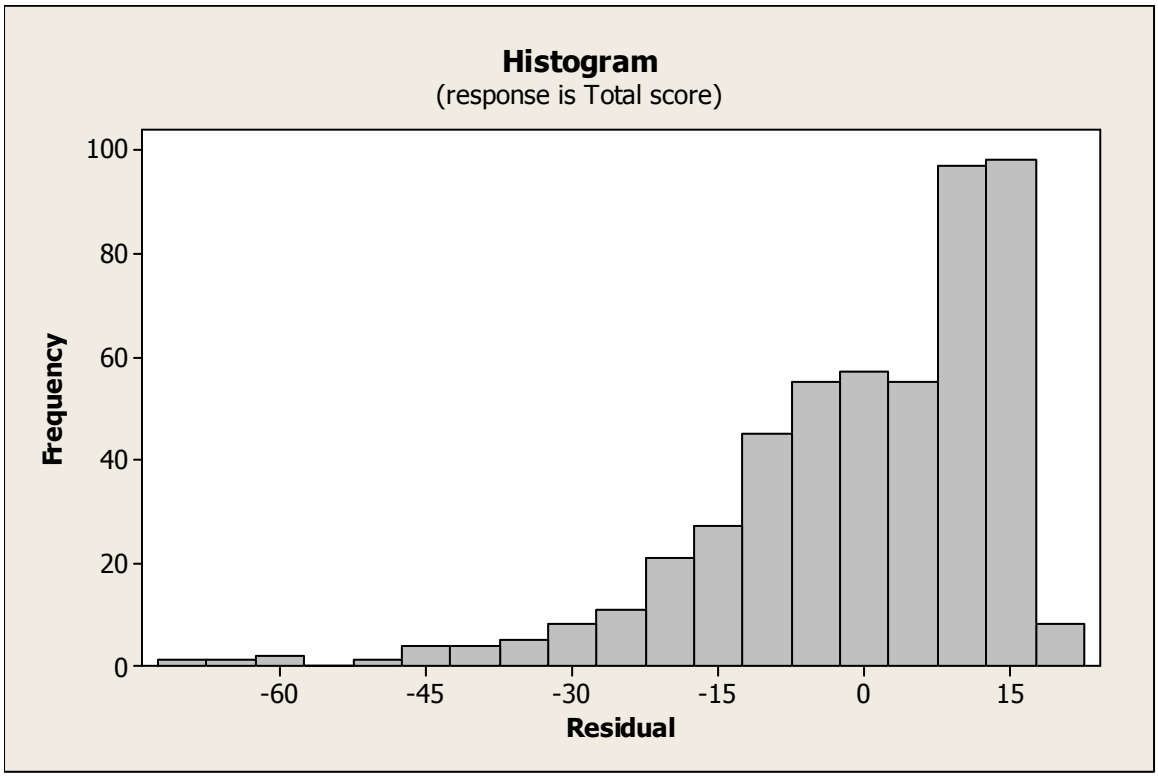
Normal Distribution curve for physical score in Peds QL 4.0



Normal Distribution curve for psychosocial score in Peds QL 4.0



Normal distribution curve for total score in Peds QL 4.0



Appendix C

The Nutrition Clinic for baseline measurements.

Appendix D

PedsQL™ Administration Guidelines[SM]

The following guidelines are intended for use by individuals trained in the administration of standardized questionnaires. The PedsQL™ administrator is crucial in developing rapport with the respondents, emphasizing the importance of the questionnaire, addressing concerns, and ensuring that the PedsQL™ is completed accurately and confidentially.

General Protocol

1. Create a procedure for assigning identification numbers that will allow for parent/child comparisons as well as comparisons of baseline/follow-up data.
2. If feasible, the PedsQL™ should be completed *before* the respondents complete any other health data forms and *before* they see their physician or healthcare provider.
3. The parent/child should first complete the PedsQL™ Generic Core Scales and then complete any additional PedsQL™ Module.
4. Parents, Children (8-12) and Teens (13-18) may self-administer the PedsQL™ after introductory instructions from the administrator. If the administrator determines that the child or teen is unable to self-administer the PedsQL™ (e.g., due to illness, fatigue, reading difficulties), the PedsQL™ should be read aloud to the child or teen. For the Young Child (5-7), the PedsQL™ should be administered by reading the instructions and each item to the young child word for word. At the beginning of each subscale repeat the recall interval instructions (one month or 7 days) to remind the young child to respond only for that specific recall interval. Use the separate page with the three faces response choices to help the young child understand how to answer. When reading items aloud to a child, intonation should be kept neutral to avoid suggesting an answer.
5. If a child has difficulty understanding the age-appropriate PedsQL™, the preceding age group version may be administered to the child (e.g., administering the Young Child (5-7) Self-Report version with the three faces response choices to an 8 year old). However, if a child presents with severe cognitive impairments (as determined by the administrator), the PedsQL™ may not be appropriate for that child. In such cases, only the Parent-Proxy Report should be administered to the child's parent.
6. The parent and child must complete the questionnaires *independently* of one another. Discourage the parent, child, or other family members from consulting with one another during the completion of the questionnaire. Let them know that they can feel free to discuss their answers following completion of the questionnaires, but that it is important to get both the parent's and the child's *individual* perspectives. If you are administering the questionnaire to the child, the child should be facing away from the parent.
7. If the child or parent has a question about what an item means or how they should answer it, do not interpret the question for them. Repeat the item to them verbatim. Ask them to answer the item according to what *they think the question means*. If they have trouble deciding on an answer, ask them to choose the response that comes closest to how they feel. The child and/or the parent has the option of not answering a question if they truly do not understand the question.
8. If a parent/child asks you to interpret the responses, tell her/him that you are not trained to interpret or provide a score for the answers given. If the PedsQL™ is being used for a clinical study, let the parent/child know that their answers will be combined with other participants' answers and analyzed as a group rather than as individual respondents.
9. Document all reasons for refusals and non-completions of the PedsQL™.

Administering the PedsQL™

1. The following scripts have been developed as a guide to introduce the PedsQL™ to the child and his/her parent(s). Modify the language to a style that is most appropriate for you and the respondent.

   For the child:

   The PedsQL™ asks you questions about how you feel and what you think about your health. It is not a test, and there are no right or wrong answers. It takes about 5 minutes to complete. If you have any questions, please let me know.

   For the parent:

   The PedsQL™ is a questionnaire that assesses health-related quality of life in children and adolescents. It contains questions about your child's physical, emotional, social, and school functioning ***in the past one month (****or for the Acute version****, in the past 7 days)****.*

   The PedsQL™ is brief and typically takes less than 5 minutes to complete. It is not a test, and there are no right or wrong answers. Please be sure to read the instructions carefully and choose the response that is the closest to how you truly feel. Please do not compare your answers with your child's responses. We are interested in your and your child's ***individual*** *perspectives. However, feel free to discuss the questionnaire with your child* ***after*** *you have both completed it and returned it to me. If you have any questions, please let me know.*

2. Provide the respondent with a pen or pencil and a solid writing surface. If a table is not available, the participant should be provided with an item such as a clipboard. Remain nearby should questions or concerns arise.
3. When the parent/child returns the PedsQL™, look it over and check to see that all answers have been completed. Verify that no item has more than one response. If any responses are incomplete, illegible, or there are multiple responses for an item, please ask the parent or child to indicate their response.
4. Ask the participants if they had any difficulties completing the questionnaire or if they have any other comments regarding the questionnaire. Document any important feedback.
5. Thank the parent and child for taking the time to complete the questionnaire. If the study design involves following up with these respondents, let them know that they may be asked to complete the PedsQL™ again at another time. Indicate when they can expect to be contacted again if known.

Christelle Berne Mapi Research Institute 27, rue de la Villette 69003 Lyon France	
Tel:	+33 (0) 472 13 66 67

رقم التعريف #_____
التاريخ_____

PedsQL™

Pediatric quality of life inventory

الطبعة 4.0 – اللغة العربية

تقرير الأطفال (8-12 سنة)

التعليمات

على الصفحه التاليه قائمة الاشياء التي قد تكون مشكلة بالنسبة لكم. من فضلك اخبرنا **كيف كان حجم المشكلة (المعاناة) التي عانيتها** خلال **الشهر الماضى** بوضع دائرة على:

0 اذا **لم تكن** هناك أية مشكلة (لا توجد معاناة)
1 اذا **غالبا لم تكن** مشكلة (نادرا ما تجدث معاناة بسيطة)
2 اذا كانت في **بعض الاحيان** مشكلة (معاناة في بعض الأحيان)
3 اذا كانت غالباً مشكلة
4 اذا كانت **تقريباً دائماً** مشكلة (بشكل شبه دائم)

في فترة الشهر الماضي، كم كانت معاناتك من المشاكل التالية

	بالنسبة لصحتي ونشاطي (مشاكل مع...)	أبداً	نادراً	بعض الأحيان	أغلب الأحيان	شبه دائم
1	من الصعب علي المسير اكثر من ربع مسافة الحي	0	1	2	3	4
2	من الصعب علي ان اركض	0	1	2	3	4
3	من الصعب علي ان امارس النشاط الرياضي او التمارين	0	1	2	3	4
4	من الصعب علي رفع شئ ثقيل	0	1	2	3	4
5	من الصعب علي ان استحم بنفسي أو أغتسل بدون مساعدة	0	1	2	3	4
6	من الصعب علي ان اقوم بأعمال منزلية	0	1	2	3	4
7	أحس بألم أو اتوجع	0	1	2	3	4
8	أحس أن طاقتي قليلة	0	1	2	3	4

	بالنسبة لمشاعري (مشاكل مع...)	أبداً	نادراً	بعض الأحيان	أغلب الأحيان	شبه دائم
1	أحس بالخوف أو الرعب	0	1	2	3	4
2	أحس بالحزن أو الإحباط	0	1	2	3	4
3	أحس بالغضب	0	1	2	3	4
4	أعاني من صعوبة بالنوم	0	1	2	3	4
5	احس بالقلق لما يمكن ان يحصل لي	0	1	2	3	4

	كيف كان تعاملي مع الآخرين (مشاكل مع...)	أبداً	نادراً	بعض الأحيان	أغلب الأحيان	شبه دائم
1	عندي مشاكل في التعامل مع الأطفال الاخرين	0	1	2	3	4
2	أقراني لا يريدون أن يكونوا اصدقاء لي	0	1	2	3	4
3	الأطفال الاخرون يضايقوني أو يسخرون مني	0	1	2	3	4
4	لا استطيع القيام بأمور يستطيع القيام بها من هم في عمري	0	1	2	3	4
5	من الصعب ملاحقة الأطفال الآخرين خلال اللعب	0	1	2	3	4

	بالنسبة للمدرسة (مشاكل مع...)	أبداً	نادراً	بعض الأحيان	أغلب الأحيان	شبه دائم
1	من الصعب التركيز في الفصل	0	1	2	3	4
2	انسى الاشياء	0	1	2	3	4
3	أعاني من صعوبة في متابعة واجباتي الدراسية	0	1	2	3	4
4	اتغيب عن المدرسة لشعوري بالتعب	0	1	2	3	4
5	اتغيب عن المدرسة للذهاب الى المستشفى او الطبيب	0	1	2	3	4

رقم التعريف #_____
التاريخ_____

PedsQL™

Pediatric quality of life inventory

الطبعة 4.0 – اللغة العربية

تقرير اليافعين (13-18 سنة)

التعليمات

على الصفحه التاليه قائمة الاشياء التي قد تكون مشكلة بالنسبة لكم. من فضلك اخبرنا **كيف كان حجم المشكلة (المعاناة) التي عانيتها** خلال **الشهر الماضى وذلك** بوضع دائرة على:

0 اذا **لم تكن** هناك أية مشكلة (لا توجد معاناة)
1 اذا **غالبا لم تكن** مشكلة (نادرا ما تجدث معاناة بسيطة)
2 اذا كانت في **بعض الاحيان** مشكلة (معاناة في بعض الأحيان)
3 اذا كانت **غالبا** مشكلة
4 اذا كانت **تقريباً دائماً** مشكلة (بشكل شبه دائم)

في فترة الشهر الماضي، كم كانت معاناتك من المشاكل التالية

	بالنسبة لصحتي ونشاطي (مشاكل مع...)	أبداً	نادراً	بعض الأحيان	أغلب الأحيان	شبه دائم
1	من الصعب المسير اكثر من مربع الحي السكني	0	1	2	3	4
2	من الصعب علي ان اركض	0	1	2	3	4
3	من الصعب علي ان امارس النشاط الرياضي او التمارين	0	1	2	3	4
4	من الصعب علي رفع شئ ثقيل	0	1	2	3	4
5	من الصعب علي ان استحم بنفسي أو أغتسل بدون مساعدة	0	1	2	3	4
6	من الصعب علي ان اقوم بأعمال منزلية	0	1	2	3	4
7	أحس بألم أو اتوجع	0	1	2	3	4
8	أحس أن طاقتي قليلة	0	1	2	3	4

	بالنسبة لمشاعري (مشاكل مع...)	أبداً	نادراً	بعض الأحيان	أغلب الأحيان	شبه دائم
1	أحس بالخوف أو الرعب	0	1	2	3	4
2	أحس بالحزن أو الإحباط	0	1	2	3	4
3	أحس بالغضب	0	1	2	3	4
4	أعاني من صعوبة بالنوم	0	1	2	3	4
5	احس بالقلق لما يمكن ان يحصل لي	0	1	2	3	4

	كيف كان تعاملي مع الآخرين (مشاكل مع...)	أبداً	نادراً	بعض الأحيان	أغلب الأحيان	شبه دائم
1	عندي مشاكل في التعامل مع اليافعين (المراهقين) الاخرين	0	1	2	3	4
2	أقراني لا يريدون أن يكونوا اصدقاء لي	0	1	2	3	4
3	المراهقون الاخرون يضايقوني أو يسخرون مني	0	1	2	3	4
4	لا استطيع القيام بأمور يستطيع القيام بها من هم في عمري	0	1	2	3	4
5	من الصعب مجاراة أقراني	0	1	2	3	4

	بالنسبة للمدرسة (مشاكل مع...)	أبداً	نادراً	بعض الأحيان	أغلب الأحيان	شبه دائم
1	من الصعب التركيز في الفصل	0	1	2	3	4
2	انسى الاشياء	0	1	2	3	4
3	أعاني من صعوبة في متابعة واجباتي الدراسية	0	1	2	3	4
4	اتغيب عن المدرسة لشعوري بالتعب	0	1	2	3	4
5	اتغيب عن المدرسة للذهاب الى المستشفى او الطبيب	0	1	2	3	4

رقم التعريف #_____
التاريخ_____

PedsQL™

Pediatric quality of life inventory

الطبعة 4.0 – اللغة العربية

تقرير آباء الاطفال (8-12 سنة)

التعليمات

على الصفحه التاليه قائمة الاشياء التي قد تكون مشكلة بالنسبة لابنكم أو ابنتكم. من فضلك اخبرنا **كيف كان حجم المشكلة (المعاناة) التي عانا ها (عانتها)** خلال **الشهر الماضى** بوضع دائرة على:

0 اذا **لم تكن** هناك أية مشكلة (لا توجد معاناة)
1 اذا **غالبا لم تكن** مشكلة (نادرا ما تجدث معاناة بسيطة)
2 اذا كانت في **بعض الاحيان** مشكلة (معاناة في بعض الأحيان)
3 اذا كانت **غالبا** مشكلة
4 اذا كانت **تقريباً دائماً** مشكلة (بشكل شبه دائم)

في فترة الشهر الماضي، كم كانت معاناة ابنك / ابنتك من المشاكل التالية

	بالنسبة لصحتي ونشاطي (مشاكل مع...)	أبداً	نادراً	بعض الأحيان	أغلب الأحيان	شبه دائم
1	المسير اكثر من مربع مسافة الحي	0	1	2	3	4
2	الركض	0	1	2	3	4
3	المشاركة النشاط الرياضي او التمارين	0	1	2	3	4
4	رفع / حمل شئ ثقيل	0	1	2	3	4
5	اخذ حمام / شور بنفسه	0	1	2	3	4
6	القيام بأعمال منزلية	0	1	2	3	4
7	يشعر بألم أو الوجع	0	1	2	3	4
8	يشعر أن طاقته قليلة	0	1	2	3	4

	بالنسبة لمشاعري (مشاكل مع...)	أبداً	نادراً	بعض الأحيان	أغلب الأحيان	شبه دائم
1	الاحساس بالخوف أو الرعب	0	1	2	3	4
2	الاحساس بالحزن أو الإحباط	0	1	2	3	4
3	الاحساس بالغضب	0	1	2	3	4
4	أعاني من صعوبة بالنوم	0	1	2	3	4
5	القلق لما يمكن ان يحصل له / لها	0	1	2	3	4

	التعامل مع الآخرين (مشاكل مع...)	أبداً	نادراً	بعض الأحيان	أغلب الأحيان	شبه دائم
1	التعامل مع الأطفال الاخرين	0	1	2	3	4
2	الأطفال الاخرون لا يريدون أن يكونوا اصدقاءه / صديقاتها	0	1	2	3	4
3	الأطفال الاخرون يضايقونه / يضايقونها أو يسخرون منه	0	1	2	3	4
4	لا يستطيع القيام بأعمال يقوم بها من هم في عمره / عمرها	0	1	2	3	4
5	اللحاق بالأطفال الآخرين خلال اللعب	0	1	2	3	4

	بالنسبة للمدرسة (مشاكل مع...)	أبداً	نادراً	بعض الأحيان	أغلب الأحيان	شبه دائم
1	التركيز في الصف	0	1	2	3	4
2	نسيان الاشياء	0	1	2	3	4
3	متابعة الواجبات المدرسية	0	1	2	3	4
4	التغيب عن المدرسة بسبب الشعور بالتعب أو المرض	0	1	2	3	4
5	التغيب عن المدرسة بسبب الذهاب الى المستشفى او الطبيب	0	1	2	3	4

رقم التعريف #_____
التاريخ_____

PedsQL™

Pediatric quality of life inventory

الطبعة 4.0 – اللغة العربية

تقرير آباء اليافعين (13-18 سنة)

التعليمات

على الصفحه التاليه قائمة الاشياء التي قد تكون مشكلة بالنسبة لابنكم أو ابنتكم. من فضلك اخبرنا **كيف كان حجم المشكلة (المعاناة) التي عانا ها (عانتها)** خلال **الشهر الماضي** بوضع دائرة على:

0 اذا **لم تكن** هناك أية مشكلة (لا توجد معاناة)
1 إذا **غالبا لم تكن** مشكلة (نادرا ما تحدث معاناة بسيطة)
2 اذا كانت في **بعض الاحيان** مشكلة (معاناة في بعض الأحيان)
3 اذا كانت **غالبا** مشكلة
4 اذا كانت **تقريباً دائماً** مشكلة (بشكل شبه دائم)

في فترة الشهر الماضي، كم كانت معاناة ابنك / ابنتك من المشاكل التالية

	بالنسبة لصحتي ونشاطي (مشاكل مع...)	أبداً	نادراً	بعض الأحيان	أغلب الأحيان	شبه دائم
1	من الصعب المسير اكثر من مربع الحي السكني	0	1	2	3	4
2	من الصعب الركض	0	1	2	3	4
3	من الصعب المشاركة النشاط الرياضي او التمارين	0	1	2	3	4
4	من الصعب رفع / حمل شئ ثقيل	0	1	2	3	4
5	من الصعب اخذ حمام / شور بنفسه	0	1	2	3	4
6	من الصعب القيام بأعمال منزلية	0	1	2	3	4
7	يشعر بألم أو الوجع	0	1	2	3	4
8	يشعر أن طاقته قليلة	0	1	2	3	4

	بالنسبة لمشاعري (مشاكل مع...)	أبداً	نادراً	بعض الأحيان	أغلب الأحيان	شبه دائم
1	الاحساس بالخوف أو الرعب	0	1	2	3	4
2	الاحساس بالحزن أو الإحباط	0	1	2	3	4
3	الاحساس بالغضب	0	1	2	3	4
4	صعوبة بالنوم	0	1	2	3	4
5	القلق لما يمكن ان يحصل له / لها	0	1	2	3	4

	كيف التعامل مع الآخرين (مشاكل مع...)	أبداً	نادراً	بعض الأحيان	أغلب الأحيان	شبه دائم
1	التعامل مع اليافعين (المراهقين) الاخرين	0	1	2	3	4
2	اليافعين الاخرين لا يريدون أن يكونوا اصدقاءه / صديقاتها	0	1	2	3	4
3	اليافعون الاخرون يضايقونه / يضايقونها أو يسخرون منه	0	1	2	3	4
4	لا يستطيع القيام بأعمال يقوم بها من هم في عمره / عمرها	0	1	2	3	4
5	مجاراة اليافعين الاخرين	0	1	2	3	4

	بالنسبة للمدرسة (مشاكل مع...)	أبداً	نادراً	بعض الأحيان	أغلب الأحيان	شبه دائم
1	التركيز في الفصل	0	1	2	3	4
2	نسيان الاشياء	0	1	2	3	4
3	متابعة الواجبات المدرسية	0	1	2	3	4
4	التغيب عن المدرسة بسبب الشعور بالتعب أو المرض	0	1	2	3	4
5	التغيب عن المدرسة بسبب الذهاب الى المستشفى او الطبيب	0	1	2	3	4

Appendix E

Published papers

Boodai and Reilly *BMC Pediatrics* 2013, **13**:105
http://www.biomedcentral.com/1471-2431/13/105

BMC Pediatrics

RESEARCH ARTICLE Open Access

Health related quality of life of obese adolescents in Kuwait

Shurooq A Boodai[1*] and John J Reilly[2]

Abstract

Background: Obesity impairs health related quality of life (HRQL) in adolescents, but most evidence in this area has mostly come from western societies. We wanted to test the hypothesis that obesity impairs HRQL in Kuwaiti adolescents, and to test for differences in HRQL assessed by self-report and parent-proxy report.

Methods: In 500 Kuwaiti 10–14 year olds HRQL was assessed using the Peds QL™ with both adolescent self-reports (n = 500) and parent-proxy reports (n = 374).

Results: Obesity was not significantly associated with HRQL in regression analysis. In a paired comparison of 98 pairs of obese adolescents vs. 98 healthy weight peers, impairment of HRQL reached significance only for physical score (95% CI = −1.5, -9.4), not for psychosocial score or total score. In a paired comparison of parent-proxy vs. self-reports for the obese adolescents, total score (95% CI = −4.9, -10.9), physical score (95% CI = −3.2, -11.0), and psychosocial score (95% CI = −4.2, -10.8) were all significantly lower in the parent reports.

Conclusions: Obesity is not associated with marked impairment of HRQL in adolescents in Kuwait, in contrast to studies in western societies. This may reflect cultural differences in attitudes towards obesity.

Keywords: Obesity, Adolescent, Health-related quality of life

Background

It is now well established, from systematic review and meta-analysis, that obesity impairs health-related quality of life (HRQL) of children and adolescents from western societies [1,2]. There is much less evidence on the extent to which obesity might impair HRQL in adolescents from non-western societies [3-7], but obesity-associated impairment of HRQL has emerged in children, adolescents, and young adults in Malaysia, Taiwan, and Lebanon [3,5-7].

It has been suggested that the impact of child or adolescent obesity on HRQL is influenced by culture [3], but since the evidence base on impairment of HRQL in adolescents is still very limited in geographical scope the hypothesis that culture influences the obesity associated impairment of child or adolescent HRQL has not been tested. For example, it is not clear whether obesity impairs the HRQL of adolescents in the Arabian Gulf States. Deficits in HRQL may drive healthcare utilization by creating a demand for obesity treatment [8-10], and understanding the extent of these deficits in non-western societies is important. One complication is differences in perceptions of HRQL between adolescents and their parents [2,3,10]. The literature suggests that the older the child, the larger the level of disagreement between the self-report and proxy-report of HRQL [11,12]. A full understanding of the impact of obesity on HRQL therefore requires that both the parent proxy-reported and adolescent- reported HRQL are considered [11-17].

The primary purpose of the present study was therefore to test the hypothesis that obesity is associated with impaired HRQL in Kuwaiti adolescents, as in western societies. A secondary aim was to test whether HRQL differed between self-reports and parent-proxy reports for the obese adolescents.

Methods

Measurement of HRQL

The Pediatric Quality of Life Inventory (PedsQL™ 4.0, MAPI Research Institute, Lyon, France) was used in the present study, with the Arabic Generic Version. The

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PedsQL™ is a generic HRQL questionnaire that has both self- and parent-proxy report forms [16]. The forms are available in age-appropriate versions (5-7 years, 8-12 years and 13-18 years), and we used the version appropriate to the age of each study participant in the present study. The PedsQL™ 4.0 is well-established, has been used most commonly in studies of child and adolescent obesity [2], and is a valid and reliable tool which is responsive to clinical change over time [16,17]. The Arabic Generic version of the PedsQL™ used in the present study is valid and reliable, e.g. with internal consistency for the different scales of 0.88-0.92 [18].

The PedsQL™ measures a multidimensional construct that includes 23 items consisting of physical, emotional, social and school performance domains from which a total score, psychosocial score (composite of the emotional function, social function, and school function domains), and physical score are derived. Items are linearly transformed to a 0 to 100 scale, so that the higher the score, the better the HRQL.

Study participants

The sample was recruited from public (state) schools in Kuwait city, the capital of Kuwait. The original intention was to recruit adolescents from a random sample of public schools, but this proved not to be possible due to limited consent to participate from school head teachers. The Ministry of Education granted approval to the research team to invite all 80 intermediate schools in Kuwait City to participate in the study. Kuwait City has 41 male public intermediate schools and 39 female public intermediate schools. Only 10/80 intermediate school head teachers responded, from 3 girls schools and 7 boys schools, and of these 10, permission to conduct the study at school was granted by only three schools; two male and one female school. Participants and their families provided informed written consent. The PedsQL™4.0 Arabic version was completed independently by the adolescents at school and by their parents at home. The study was approved by the Medical Research Committee of the Ministry of Health and the Ethical Committee of the Ministry of Education in Kuwait.

Study participants were included if within the eligible age range (within grades 5–9, the grade range for intermediate schools, age 10 to 14y), and were either obese or healthy weight as defined below. Overweight pupils were excluded from the study sample in order to provide a marked contrast in weight status between the two groups of interest, and to minimize the impact of any mis-classification arising from use of the body mass index. Other exclusions were based on a brief medical history/checklist aimed at including only apparently healthy adolescents, and excluding participants with serious chronic or acute illness which might affect their HRQL.

Assessment of weight status and formation of obese-healthy weight matched pairs

From the three schools which agreed to participate, screening of weight status to determine eligibility was carried out in a total of 1042 pupils (542 boys, 500 girls). Pupils were categorised into healthy weight, overweight, and obese groups relative to reference data from the US CDC 2000 [19]. Obesity was defined as BMI ≥ 95th centile, overweight as BMI of ≥ 85th centile and <95th centile, healthy weight was defined as BMI ≥ 3rd centile and < 85th centile. The US BMI reference data were used in the present study because the absolute BMI values at standard Kuwaiti centiles are extremely high [20], as the Kuwaiti BMI reference was constructed after the obesity epidemic had affected Kuwait [21]. The total number of pupils who did not fulfill the inclusion criteria and/or did not consent was 542, 224 males and 318 females, leaving 500 eligible consenting participants, 318 boys and 182 girls.

A pre-planned paired analysis of HRQL between obese and healthy weight participants, with pair matching for same sex, same school, same school year, and same ethnic group (all participants were Kuwaiti nationals) yielded 98 pairs with 57 paired comparisons in boys and 41 paired comparisons in girls.

Statistical analysis

All statistical analyses were performed using Minitab 16.0. Data were checked for normality by descriptive statistics and histograms with normal distribution curves. Both the descriptive data, and differences between groups (e.g. between self versus parent reports) were non-normally distributed and so non-parametric statistical tests were used. For the whole sample self-reports, the skewness and kurtosis values for the physical score were −1.10 and 1.70 , for the psychosocial score these were −1.42 and 2.48 and for the total score they were −1.14 and 1.07 , respectively. For the parent-proxy reports, skewness and kurtosis values for the total score were −0.49 and −0.66, for the psychosocial score −0.44 and −0.51, and for the physical score were −0.84 and −0.30, respectively.

In order to test whether obesity was associated with impaired HRQL two statistical approaches were taken. First, multiple regression was used with HRQL (total score, physical score, and psychosocial score) as the outcome and age, gender, and weight status as the explanatory variables. Second, paired comparisons were undertaken between obese versus healthy weight study participants. Wilcoxon signed-rank tests were used to determine the significance of differences in the paired scores between the obese and the healthy weight groups.

We also used Wilcoxon signed-rank tests to determine the significance of any difference in scores between adolescent self-reports and parent-proxy reports in the obese group.

Results

Sample characteristics

The final study sample consisted of 500 adolescents, 224 obese and 276 healthy weight, 318 boys (63.6%) and 182 girls (36.4%), median age 12.3y. Of the 500 adolescent participants self- reports were available from all 500, but parent-proxy reports were available from 162 of the obese group and 212 from the healthy-weight group. Characteristics of study participants are summarized in Table 1.

Test of the hypothesis that HRQL is impaired in the obese group: multiple regression analysis

Of the potential explanatory variables of age, gender, and weight status, only gender had a significant influence on adolescent self-reported HRQL (n = 500; significantly lower total score in girls than boys, p =0.02). In parent-proxy reports, age (lower in older than younger participants, $p < 0.01$) and gender (lower in girls than boys $p < 0.01$) had a significant impact on total score. There was no evidence that obesity was associated with impaired HRQL (total score, physical score, psychosocial score) in the regression analyses.

Test of the hypothesis that HRQL is impaired in the obese group: paired comparisons of obese versus healthy weight participant

Demographic information Formal matched pairs were selected from the obese and healthy weight groups (n = 98 pairs). Median (IQR) ages of the healthy weight and obese groups were both 12.4 (2.1). Median (IQR) BMI Z scores were 0.1 (1.1) for the healthy weight group and 2.1 (0.4) for the obese group.

Self-reports Summary data are shown in Table 2. There was no significant difference in the total score between groups (n =98 pairs), but the physical score for the healthy weight group was significantly higher than in the obese group.

Parent-proxy reports As shown in Table 2, there were no significant differences in the paired comparisons of parent-proxy reports between the obese group and healthy weight group.

Differences between self-reports and parent-proxy reports for the obese adolescents

There were 162 obese adolescents for the paired comparisons between self-reports and parent-proxy reports (median age = 12.4y, IQR =2.1). Parent-proxy reports were significantly lower than self-reports for physical score (95% CI = 3.2, 11.0), psychosocial score (95% CI = 4.2, 10.8), and total score (95% CI = 4.9, 10.9).

Discussion

The primary aim of the present study was to test whether the impairment of 'total' HRQL associated with obesity from western samples, as measured by the PedsQL™, [1,2] was present in a community sample of adolescents from Kuwait. The results do not suggest that obesity impairs total HRQL markedly in Kuwaiti adolescents, in contrast to findings from western samples [1,2] and some non-western samples [3-7].

Table 1 Characteristics of study participants, median (IQR)

Variable	Healthy weight group			Obese group		
	Boys	Girls	Total	Boys	Girls	Total
	n = 176	n = 100	n = 276	n = 142	n = 82	n = 224
Age	12.3 (2.2)	12.2 (2.3)	12.3 (2.2)	12.6 (1.8)	12.4 (2.1)	12.4 (2.0)
BMI (kg/m^2)	18.0 (2.9)	18.2 (2.9)	18.1 (3.0)	28.7 (6.8)	29.3 (4.9)	28.8 (5.5)
BMI Z score	0.0 (1.2)	0.1 (1.0)	0.1 (1.1)	2.1 (0.4)	2.0 (0.4)	2.1 (0.4)
HRQL Self-report						
Physical score	96.9 (15.6)	87.5 (19.7)	93.7 (18.8)	90.6 (21.9)	81.3 (28.9)	87.5 (25.0)
Psychosocial score	90.0 (21.6)	86.7 (23.4)	88.3 (20.0)	87.5 (18.4)	82.5 (21.6)	85.0 (18.3)
Total score	92.4 (19.5)	86.4 (20.6)	89.1 (20.3)	88.0 (18.4)	79.3 (21.2)	84.8 (21.2)
HRQL Parent-proxy report	n = 125	n = 87	n = 212	n = 91	n = 71	n = 162
Physical score	90.6 (25.0)	75.0 (43.7)	87.5 (34.4)	84.4 (31.3)	81.3 (43.8)	82.9 (34.4)
Psychosocial score	78.3 (25.0)	70.0 (28.4)	76.7 (26.7)	76.7 (20.0)	80.0 (29.9)	76.7 (25.0)
Total score	82.6 (22.3)	69.6 (31.6)	79.3 (29.3)	76.1 (21.7)	81.5 (29.3)	78.3 (25.3)

Table 2 Paired comparisons of Health Related Quality of Life (HRQL) for the healthy weight group vs. obese group, median (IQR)

Variable	Healthy weight group n = 98	Obese group n = 98	95% CI	*P-value*
Self-report	Median (IQR)	Median (IQR)		
Physical score	90.6 (18.7)	87.5 (31.2)	1.5, 9.4	0.007
Psychosocial score	88.3 (18.3)	85.0 (20.4)	−1.6, 7.5	0.224
Total score	88.0 (17.7)	84.8 (25.0)	−0.5, 7.1	0.087
Parent-proxy report				
Physical score	86.0 (40.6)	81.3 (31.3)	−4.7, 6.3	0.756
Psychosocial score	76.7 (25.0)	76.7 (28.3)	−3.4, 5.8	0.773
Total score	79.3 (31.5)	78.8 (24.5)	−2.8, 6.0	0.550

Median (IQR) ages of healthy weight and obese groups were both 12.4y (2.1). Median (IQR) BMI Z scores were 0.1 (1.1) for the healthy weight group, and 2.1 (0.4) for the obese group.

The present study did find evidence of a deficit in the physical health domain of HRQL , but not for the psychosocial health domain .It is possible that the physical health effects of adolescent obesity might be more universal than psychosocial effects, Psychosocial effects of obesity might be more sensitive to cultural differences, e.g. in the perception of obesity. The apparent lack of impact of obesity on the psychosocial domain of HRQL in the present study might reflect cultural differences in the perception of obesity between Kuwait and western societies, but further research would be required to confirm this. The community-based nature of the sample might also have reduced any potential HRQL deficits associated with obesity. It is possible that HRQL is more greatly impaired in clinic based, treatment-seeking samples [5,6,8,9].

Recent systematic reviews have noted that almost all of the evidence reviewed has been from western countries [1,2]. Very recently, some evidence has begun to emerge from non-western societies [3-7] and this has generally supported the hypothesis that child or adolescent obesity is also associated with reduced HRQL in non-western cultures. The most relevant comparison to the present study is from studies using the PedsQL™ in Arab countries, but such studies are very scarce. Fazah et al. [7], in a community sample of Lebanese 14–18 year olds found that obesity was associated with HRQL impairment, but only in females not males. In contrast, most of the evidence from western societies, as summarized in a recent systematic review [2], suggests that obesity-associated impairment of HRQL applies to both sexes.

We are aware of only one previous study of HRQL in adolescents and young adults in Kuwait: Al-Fayez and Ohaeri [22] used a different instrument to measure HRQL and included older participants than those recruited to the present study, 14-23 y olds. In the study by Al-Fayez and Ohaeri [22] HRQL scores were lower than in samples from western countries, lower in females than males, but the influence of obesity on HRQL was not considered. The reasons why HRQL is lower in girls than boys was not the main focus of the present study, but was consistent with the findings of Al-Fayez and Ohaeri [22].

The secondary aim of the present study was to test the hypothesis that parent-proxy and self- reports of HRQL might differ in obese adolescents. The present study showed that parent-reported HRQL was significantly lower than adolescent-reported HRQL, this emphasizes the potential value of obtaining both parent and self-reports of HRQL [23-25]. Most previous studies have also found that parent-proxy scores for HRQL in obese children and adolescents are lower than scores from self-reports [2]. A detailed discussion of differences in HRQL between parent-proxy versus self reports is beyond the scope of the present manuscript, but a number of detailed studies of the topic have been published [11-15]. The present study simply aimed to establish whether HRQL scores differed between parents and their obese adolescent offspring.

The novelty of the study setting (Arabian Gulf), relatively large sample, heterogeneity of the sample, and ability to compare HRQL between obese versus healthy weight adolescents, were the main study strengths.

The present study also had a number of weaknesses. While the sample size was larger than in many previous studies included in recent systematic reviews [1,2], the school response rate was disappointing and no random selection of schools was possible. In the present study it was not practical to characterize the excluded participants in detail, nor to assess pubertal stage of study participants, yet an assessment of maturation might have added to the information available from chronological age. Most of the psychosocial co-morbidities of child and adolescent obesity tend to worsen with age and/or developmental stage [26]. The present study also focused specifically on HRQL, and cannot address the wider psychosocial co-morbidities of adolescent obesity [1,25-29]. In the present study we were unable to consider all potential influences on HRQL, e.g. we had no measure of socio-economic status (SES) which has a weak association with HRQL in young adults in Kuwait [22], but since the sample was relatively homogenous (same ethnicity, narrow age range, from the same small number of public schools) the range in SES was probably relatively narrow. In our analyses based on paired comparisons of obese and healthy weight adolescents, members of each

pair were from the same school year, same sex, and also from the same school. This high degree of pair-wise matching should have minimized the impact of differences other than obesity between the pairs. We were unable to consider any impact of overweight on HRQL, as distinct from obesity, since we excluded the overweight in order to establish adequate contrast between obese and healthy weight groups. However, since the deficits in HRQL associated with obesity in the present study were so small it seems likely that deficits in HRQL associated with overweight might be even smaller. The cross-sectional design of the present study was also a limitation, though most of the research in this area to date has also been cross-sectional [1,2]. Finally, while we did not test the psychometric properties of the PedsQL™ in our sample, in previous studies these have been consistently very positive [7,15-18].

Conclusion

In conclusion, the present study suggests that adolescent obesity is not associated with marked impairment of HRQL in Kuwait, in contrast to what would have been expected from previous studies of largely western samples. This finding suggests that cultural differences might modify the impact of obesity on HRQL among adolescents.

Competing interests

The authors have no conflicts of interest to declare.

Author contributions

Both authors were involved in concept and study design; both drafted the manuscript and revised for critical intellectual content; both gave final approval for submission.

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TRIALS

RESEARCH Open Access

National Adolescent Treatment Trial for Obesity in Kuwait (NATTO): project design and results of a randomised controlled trial of a good practice approach to treatment of adolescent obesity in Kuwait

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Abstract

Background: Few randomised controlled trials (RCTs) of interventions for the treatment of adolescent obesity have taken place outside the western world. This RCT tested whether a simple 'good practice' intervention for the treatment of adolescent obesity would have a greater impact on weight status and other outcomes than a referral to primary care (control) in adolescents in Kuwait City.

Methods: We report on an assessor-blinded RCT of a treatment intervention in 82 obese 10- to 14-year-olds (mean age 12.4, SD 1.2 years), randomised to a good practice treatment or primary care control group over 6 months. The good practice intervention was intended as relatively low intensity (6 hours contact over 24 weeks, group-based), aiming to change sedentary behaviour, physical activity, and diet. The primary outcome was a change in body mass index (BMI) Z score; other outcomes were changes in waist circumference and blood pressure.

Results: The retention of subjects to follow up was acceptable (n = 31 from the intervention group, and n = 32 from the control group), but engagement with both the intervention and control treatment was poor. Treatment had no significant effect on BMI Z score relative to control, and no other significant benefits to intervention were observed.

Conclusions: The trial was feasible, but highlights the need to engage obese adolescents and their families in the interventions being trialled. The trial should inform the development of future adolescent obesity treatment trials in the Gulf States with the incorporation of qualitative assessment in future intervention trials.

Trial registration: RCT Registered as National Adolescent Treatment Trial for Obesity in Kuwait (NATTO): www.controlled-trials.com/ISRCTN37457227, 1 December 2009.

Keywords: obesity, overweight, adolescents, treatment, BMI, randomised controlled trial

Background

Prevalence of child and adolescent obesity has increased dramatically in recent years in Kuwait, [1,2], as in much of the rest of the world. While prevention of obesity is paramount, most preventive interventions have had only a modest impact, and there is a need to offer weight management interventions for adolescents who are already obese [3,4], particularly given the large number of serious short-term and long-term co-morbidities of adolescent obesity [5,6].

Despite the importance of treatment interventions for adolescent obesity, recent systematic reviews have found almost no evidence on treatment interventions outside the western world [3]. Specifically, the recent Cochrane review [3] found 29 eligible trials of adolescent obesity treatment, and none of these were from the Arab world (16 from North America, 7 from Europe and Australia; 3 from Asia; and 2 from Israel). The primary aim of the present study

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was therefore to test the hypothesis that a 'good practice' intervention for the treatment of adolescent obesity in Kuwait would have a greater effect on primary and secondary outcomes than allocation to a control group. The secondary aims were to test the feasibility of conducting such a trial in Kuwait and to test the feasibility of using a good practice intervention and referral to primary care as a control condition, with a view to developing improved obesity treatment RCTs in Kuwait and the other Gulf States.

Methods

Participants

The study was conducted at Al Faiha polyclinic (primary care clinic) during 2009. For entry into the study, adolescents, ages 10 to 14 years had to be obese (body mass index (BMI) above the 95th percentile [7]), have at least one parent who expressed a willingness to attend the intervention described below if allocated to it, and have no serious underlying medical condition that might be either a cause or consequence of their obesity. Adolescents were recruited from their schools after BMI and health screening was conducted by one of the researchers (SAB). The schools and residences of all participants were located in the capital, and both the venue for the intervention (Al Faiha polyclinic) and the venue for the control primary care clinic were also in the capital to ensure that distance was not an issue hindering attendance. Ethical approval was obtained from the Ethics Committee for Medical Research, Ministry of Health of Kuwait (ref MPH/112), and written informed consent was obtained from both parents and adolescents.

Randomisation and allocation concealment

Participating adolescents attended a research clinic where all baseline measures (see below) were taken, then assigned a unique study code prior to random allocation into the treatment or control group. To ensure concealment of allocation, codes were sent electronically to a statistician (JHM) who produced a computer generated randomisation list that allocated participants to intervention or control group, with participants balanced for gender in blocks of 10. The statistician informed the researcher responsible for delivering the intervention (SAB) of the allocation, and families were invited to intervention or control groups as appropriate.

Intervention

In brief, the intervention was intended as a relatively low intensity (6 sessions, 1 hour contact time per session, delivered as a group session) programme, which might be readily generalisable if evidence of feasibility and efficacy was obtained from the present study. The intervention was delivered to the adolescents and their parents in group-discussion fashion over a 24-week period by a physician with specialist training in Nutrition (SAB) and the study dietician. The programme was adapted from the Scottish Childhood Obesity Treatment Trial (SCOTT), which tested a 'good practice' treatment intervention in Scotland [8,9]. Parents were provided with treatment materials that were adapted from those used in SCOTT [9]. The intervention is described here as a 'good practice' intervention on two grounds. First, because it focused on changing the behaviours recommended as the key targets in recent evidence-based management guidelines [10-12] for the treatment of adolescent obesity (reduction in sedentary behaviour, particularly screen-media use; diet, using a modified version of the 'traffic light diet' system [8]; and promotion of physical activity). Second, the intervention incorporated theoretically based behaviour change techniques to all three of the targeted behaviours [8]: exploration of the pros and cons of changes in diet, physical activity, and sedentary behaviour; exploration of motivation to change diet, physical activity, and sedentary behaviour; self-monitoring of sedentary behaviour (recording of screen time in diaries), diet, and physical activity (recording of walking, sport, and physically active play in a diary); identifying the main barriers to behaviour change and problem solving in relation to these barriers; goal setting in relation to diet, physical activity, and sedentary behaviour; and relapse prevention.

The intervention group was further divided into boys (n = 21, each attending with at least one parent) and girls (n = 20, each attending with at least one parent) groups in accordance with cultural norms of the Kuwaiti population, and their sessions were delivered on two consecutive days. Any adolescent who attended the intervention session alone was welcomed, although ideally at least one parent should have been present.

Control group

Primary care-based treatment of child and adolescent obesity in Kuwait is somewhat limited, as in many other countries, but it was felt ethically and scientifically appropriate to use referral to primary care as a control condition in the present study. Adolescents, and their parents, who were allocated randomly to the control group were therefore informed that they were obese and advised to attend primary care.

Outcome measures and blinding

BMI Z scores were calculated based on US CDC 2000 reference data [7] using the software available at http://stokes.chop.edu/web/zscore/index.php. Outcome measures were made at baseline and again at 6 months (26 weeks) after the start of the intervention by the same trained research assistants who were blinded to group allocation and were not involved in delivery of the treatment intervention. Blood pressure was measured when the participant was sitting quietly in the upright position, with the correct

cuff size applied to the right arm. The reading was repeated three times and the average of the three readings was taken.

The primary study outcome measure was change in BMI Z score. Weight was measured to 0.1 kg in light indoor clothing with children not wearing shoes, and height was measured to 0.1 cm with a portable stadiometer (Leicester Height Measure, SECA, London, UK) and adolescents not wearing shoes. Secondary outcomes were waist circumference and blood pressure.

Sample size, power, and statistical analysis

No local data were available upon which to base a power calculation. The present study was therefore powered using BMI data from the Scottish SCOTT RCT [8], which was used to develop the treatment intervention. With a between-group difference in the change in BMI Z-score of -0.25 at 6 months (which is a small change in BMI Z score, as discussed below) and a SD of change in BMI Z score of 0.21, giving a delta of 1.15, a sample size of around 30 adolescents per arm at 6 months would give 90% power at the 0.05 significance level. Dropout from the trial could not be predicted, but it was hoped that entering around 90 adolescents would make sufficient allowance for attrition during the 6-month study to leave around 30 participants per arm at the end of the trial.

Outcomes were analysed in two ways. First, changes in outcome variables within each group (intervention and control) between baseline and 6-month follow-up are presented. The issue of whether changes in outcome variables differed significantly between groups (intervention versus control) was examined using independent sample t-tests. The analysis was intention-to-treat, where we used data from all adolescents for whom data were available on the basis of the group to which they were allocated, regardless of their adherence to the protocol (attendance).

Feasibility of the trial: treatment intervention and control conditions

Since the present study was the first of its kind in Kuwait, it was not considered as a 'definitive trial' [13] but rather as the initiation of a process which should lead to a more definitive trial subsequently [13]. Feasibility of the trial and feasibility of the trial interventions were measured by summarising the extent of sample attrition (dropout) over the 6-month period, the extent of missing data, and recording attendance at intervention and control treatments.

Results

Flow of participants through the trial, flow through the interventions, and participant characteristics

Figure 1 describes the flow of participants through the trial and through the intervention. Of the 82 participants entered at baseline, 63 (77%) attended for outcome measures at the 6-month follow-up. There were no significant differences at baseline between intervention and control groups for adolescent age, anthropometric measures and weight status (Table 1).

Changes in primary and secondary outcomes within and between groups

Table 2 provides data on change in BMI Z scores, blood pressures and waist circumference. There were no statistically significant differences within the two groups over the 6 months for any of the anthropometric measures. There were also no significant differences between the groups for the 6-month changes in anthropometry (Table 2). Only 7 of the 31 adolescents in the intervention group at the end of the study maintained or lost weight over the 6 months, while 5/32 in the control group maintained or lost weight over the 6 months.

Discussion

Main findings, study implications, and comparisons with other evidence

While it seems that no previous adolescent obesity treatment RCTs have been published from Kuwait or the other Gulf States, the present study suggests that conducting randomised controlled trials of adolescent obesity treatment interventions in Kuwait is feasible. Retention in the trial was acceptable and not strikingly dissimilar to that reported in other adolescent obesity treatment trials that took place over a similar timescale [3]. Luttikhuis and colleagues in the recent Cochrane review described attrition in the eligible adolescent obesity treatment trials (of at least 6 months duration) as ranging from 0 to 43% by the end of the intervention [3]. An expansion of the evidence base on interventions to treat adolescent obesity is required because most obese adolescents now live outside western countries [14]. However, the recent Cochrane review [3] found no eligible RCT from the Arab world.

The present study also suggests that adherence to obesity interventions in obese adolescents and their families in Kuwait might be very poor. While retention in the trial was acceptable, engagement with the interventions offered was limited: only 12 participants (29% of the sample) attended ≥4 sessions, and the control group families did not attend any sessions at primary care. The reasons for poor adherence to both the study intervention and control treatments are probably complex and a detailed discussion of them is beyond the scope of the present study. However, a number of the adolescents and their families expressed a low degree of concern about obesity on being given the diagnosis and at the treatment sessions which they attended, and the poor attendance is consistent with this view. The fact that attendance was negligible even in the control group implies a low degree of concern about obesity rather than any specific non-engagement with the

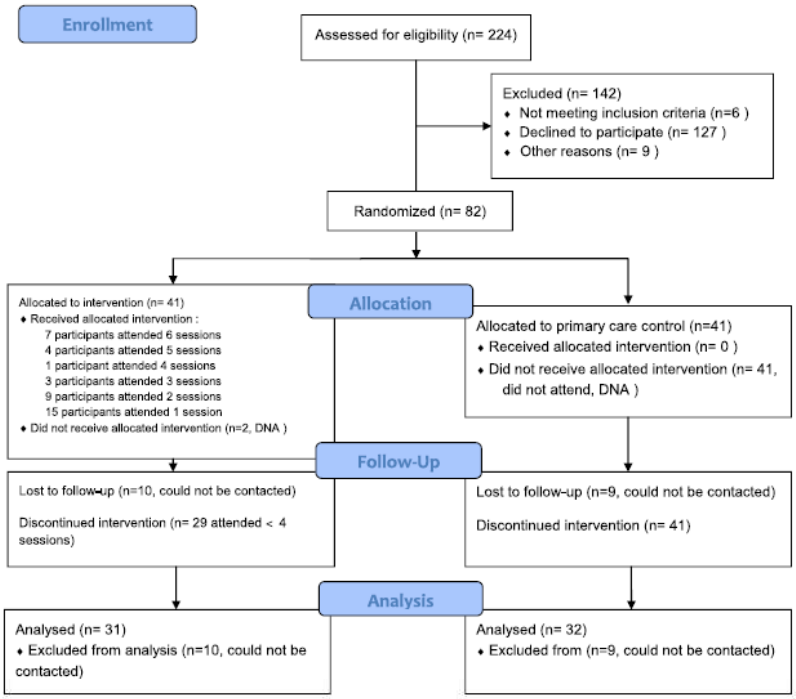

Figure 1 CONSORT 2010 flow diagram.

intervention arm of the trial. In a recent study of adolescents in Kuwait city [15] we reported that health-related quality of life was not impaired in obese adolescents relative to their healthy weight peers; this is an unusual finding [16,17], and it seemed to reflect a cultural difference between western and Kuwaiti societies, with a reduced concern over obesity in Kuwait [15]. Of note, we analysed blood samples from 80 out of the 82 participants in NATTO for cardiometabolic risk factors at baseline; however, results of the analyses were only available after the end of the trial. Had these results been available, they may have had an impact on the motivation to attend of both the intervention and the control groups. Several studies have shown multiple cardiometabolic risk factors in obese adolescents both in Kuwait [18] and internationally [19,20].

Exploring the reasons for non-attendance and non-adherence to treatment and investigating the treatment preferences of obese adolescents and their families would be important for future adolescent obesity treatment research

Table 1 Characteristics of participating adolescents at baseline

Characteristic	Full sample n = 82 Mean (SD)	Treatment group n = 41 Mean (SD)	Control group n = 41 Mean (SD)
Age (years)	12.4 (1.2)	12.4 (1.2)	12.4 (1.2)
Male/female	42/40	21/20	21/20
Body mass index Z score	2.2 (0.3)	2.2 (0.3)	2.2 (0.3)
Systolic blood pressure (mmHg)	122.2 (10.4)	122.0 (12.3)	122.0 (8.2)
Diastolic blood pressure	77.5 (7.6)	76.0 (8.5)	79.1 (6.4)
Waist circumference (cm)	93.5 (12.1)	93.0 (12.7)	94.0 (11.6)

Attendance at the intervention group and control group sessions was low and is shown in Figure 1.

Table 2 Six-month changes in outcome measures within and between-groups (n = 31 treatment group versus 32 controls)

Outcome	Intervention group within-group change mean (SD)	Control group within-group change mean (SD)	Between-group difference, mean (95% CI), *P* value
Body mass index Z score	0.0 (0.1)	0.0 (0.2)	0.0 (-0.1; 0.1), 0.6
Systolic blood pressure (mmHg)	0.4 (6.7)	0.6 (4.8)	0.3 (-2.7; 3.2), 0.9
Diastolic blood pressure (mmHg)	2.9 (6.2)	1.1 (5.8)	-1.8 (-4.8, 1.3), 0.2
Waist circumference (cm)	4.9 (5.8)	3.5 (5.7)	-1.4 (-4.3; 1.5), 0.3

in Kuwait and the other Gulf States. Indeed, the UK Medical Research Council Framework on the Development and Evaluation of Complex Interventions [13] recommends an approach in which interventions are developed in conjunction with study participants, and qualitative studies are used to understand treatment preferences.

The degree of change in body weight status that might be desirable in an adolescent obesity treatment intervention is uncertain [10-12], but improvements in cardiometabolic risk factors probably require much greater changes than were observed in the present study, [21,22]. Weight maintenance or modest weight loss is usually recommended for adolescent obesity treatment interventions [10-12], but in the present study, only a minority of participants maintained or lost weight. Since adherence to treatment ranged from limited to absent in the present study, the actual 'dose' of obesity treatment was probably also very low, amounting to little more than the confirmation to the adolescents and their families that they were obese with some evidence-based advice. The present study is therefore consistent with some others (for example, [23]) in suggesting that diagnosis of obesity plus good advice alone is likely to have null or minimal effects on energy balance of obese adolescents.

Study strengths and weaknesses

The principal strengths of the present study were the high level evidence obtained, with adherence to the CONSORT statement on conduct and reporting of RCTs [24]; the fact that the trial was powered adequately, in contrast to a number of previous trials in this area [3]; development and testing of a potentially generalisable intervention; and completing a challenging adolescent obesity treatment RCT [25] in the novel setting of a Gulf State.

The present study also had a number of weaknesses. Longer term obesity treatment trials are desirable, and a 6-month follow-up is considered the minimum desirable in the most recent Cochrane review of paediatric obesity treatment RCTs [3]. An assessment of parent and adolescent perspectives on the treatment programme would have been desirable in order to both understand the current intervention better and to inform future treatment interventions [13,26,27]. Future intervention trials in Kuwait might also find it useful to focus treatment at other population subgroups (for example, younger or older participants, or to tailor treatment to boys or to girls), but this was not possible in the present study due to resource limitations.

Conclusions

The present study suggests that trials of obesity treatment interventions in adolescents in Kuwait are feasible, but that the success of future trials will depend on addressing the problem of low adherence to treatment.

Abbreviations

BMI: body mass index; BMI Z score: body mass index Z score; CONSORT: consolidated standards of reporting trials; RCT(s): randomised controlled trial(s); SD: standard deviation.

Competing interests

The authors declare that they have not competing interests.

Authors' contributions

SAB: Conception and design, data collection and analysis, manuscript writing and final approval. JHM: Design, analysis, critical revision and final approval of the manuscript. JJR: Conception and design, manuscript writing and critical revision and final approval of the manuscript. All authors read and approved the final manuscript.

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ORIGINAL RESEARCH

Prevalence of cardiometabolic risk factors and metabolic syndrome in obese Kuwaiti adolescents

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Background: Childhood and adolescent obesity is associated with insulin resistance, abnormal glucose metabolism, hypertension, dyslipidemia, inflammation, liver disease, and compromised vascular function. The purpose of this pilot study was to determine the prevalence of cardiometabolic risk factor abnormalities and metabolic syndrome (MetS) in a sample of obese Kuwaiti adolescents, as prevalence data might be helpful in improving engagement with obesity treatment in future.

Methods: Eighty obese Kuwaiti adolescents (40 males) with a mean (standard deviation) age of 12.3 years (1.1 years) participated in the present study. All participants had a detailed clinical examination and anthropometry, blood pressure taken, and assessment of fasting levels of C-reactive protein, intracellular adhesion molecule, interleukin-6, fasting blood glucose, insulin, liver function tests (alanine aminotransferase, aspartate aminotransferase, gamma glutamyltransferase), lipid profile (cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglycerides), insulin resistance by homeostasis model assessment, and adiponectin. MetS was assessed using two recognized criteria modified for use in younger individuals.

Results: The cardiometabolic risk factors with highest prevalence of abnormal values included aspartate aminotransferase (88.7% of the sample) and insulin resistance by homeostasis model assessment (67.5%), intracellular adhesion molecule (66.5%), fasting insulin (43.5%), C-reactive protein (42.5%), low-density lipoprotein cholesterol (35.0%), total cholesterol (33.5%), and systolic blood pressure (30.0%). Of all participants, 96.3% (77/80) had at least one impaired cardiometabolic risk factor as well as obesity. Prevalence of MetS was 21.3% according to the International Diabetes Federation definition and 30% using the Third Adult Treatment Panel definition.

Conclusion: The present study suggests that obese Kuwaiti adolescents have multiple cardiometabolic risk factor abnormalities. Future studies are needed to test the benefits of intervention in this high-risk group. They also suggest that prevention of obesity in children and adults should be a major public health goal in Kuwait.

Keywords: obesity, adolescents, prevalence, cardiometabolic risk factors, metabolic syndrome

Background

Childhood and adolescent obesity is associated with insulin resistance, abnormal glucose metabolism, hypertension, dyslipidemia, inflammation, liver disease, and compromised vascular function.[1–5] As with obesity, these impairments could track into young adulthood, which increases the risk of cardiometabolic diseases and even certain types of cancer independent of adult weight.[6,7]

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The detrimental effects of adolescent obesity on subsequent risk of cardiovascular disease are partly mediated by the presence of cardiometabolic risk factors.[8] Cardiovascular disease is the leading cause of morbidity and mortality worldwide with an estimate of 17.3 million deaths in 2008, and by 2030 this number could reach up to 23.3 million.[9] It is widely believed that atherosclerosis begins in childhood and progresses into adulthood.[10,11] As the number of cardiovascular disease risk factors increases in childhood, so does the severity of both coronary and aortic atherosclerosis in young adulthood.[3] In the Netherlands, two-thirds of obese children and adolescents had more than one cardiovascular disease risk factor in one study.[12] In Germany and Switzerland, around 50% of obese children had at least one cardiometabolic risk factor in one study.[13]

The presence of obesity in childhood and adolescence is also related to the development of fatty liver or steatosis, which is the most common liver abnormality in this age group.[14] Steatosis can be present with or without elevated liver enzymes (aminotransferases).[15] For the long term, the ramifications of having persistently elevated liver enzymes and steatosis are important and could lead eventually to the development of cirrhosis.[14,16]

In two previous studies of obese adolescents in Kuwait, we observed that their health-related quality of life was unimpaired compared with nonobese peers,[17] and that their engagement with therapy to treat obesity was poor.[18] It is possible that knowledge of the presence of cardiometabolic risk factors in obese adolescents may increase the engagement of adolescents and their families with efforts to treat obesity. The aim of the present study was therefore to estimate the prevalence of cardiometabolic risk factors in obese adolescents in order to provide evidence that might be useful to future obesity treatment. In the present study, we carried out assessments of obesity-related cardiometabolic risk factors that could impair vascular health and liver function. These included lipid profile (cholesterol, low-density lipoprotein [LDL], very low-density lipoprotein, high-density lipoprotein [HDL], triglycerides [TG]), interleukin-6 (IL-6), intracellular adhesion molecule (ICAM), C-reactive protein (CRP), adiponectin, liver function tests (alanine aminotransferase [ALT], aspartate aminotransferase [AST], gamma glutamyltransferase [GGT]), and insulin resistance by homeostasis model assessment (HOMA-IR).

Materials and methods

Participants

The study was the baseline element of an intervention to treat adolescent obesity using a randomized controlled trial, the National Adolescent Treatment Trial for Obesity (NATTO).[18] We recruited 80 obese adolescents participating in the NATTO in Kuwait City[18] at the preintervention stage of the trial. They were all at or above the age- and sex-adjusted 95th body mass index (BMI) percentile, which defines obesity.[19] Age ranged from 10 years to 14 years. All participants underwent physical examination including anthropometric assessment (weight, height, BMI, waist circumference) and had no medical or surgical history. All participants and their parents consented to take part in the study. The study was approved by the Medical Research Committee of the Ministry of Health – Kuwait.

Blood samples were drawn for analysis for fasting blood glucose (FBG), fasting insulin, cholesterol, LDL, HDL, TG, ALT, AST, GGT, CRP, IL-6, ICAM, and adiponectin. Insulin resistance was measured by HOMA-IR (fasting insulin × fasting glucose/22.5).[20]

Blood pressure was measured when the participant was sitting quietly in the upright position, with the correct cuff size applied to the right arm. The reading was repeated three times, and the average of the three readings was taken.

Biochemical assessment

Cholesterol, TG, HDL, sensitive CRP, ALT, AST, and GGT assays were assessed using a C311 Roche analyzer; sensitive CRP immunotubidimetric assays with cholesterol, TG, HDL, ALT, AST, and GGT being enzymatic colorimetic. Kits were supplied by Roche Diagnosticx GmbH. IL-6, ICAM, adiponectin, and insulin analysis (enzyme-linked immunosorbent assays) was assessed using kits supplied by R&D Systems Europe Ltd (Oxford, UK) and Mercodia AB.

Cutoff points for defining the cardiometabolic risk factors and metabolic syndrome

There are two commonly used cutoff points for FBG (mmol/L), the World Health Organization (WHO) normal cutoff <6.1 mmol/L[21] and the American Diabetes Association normal cutoff <5.6 mmol/L.[22] However, in Kuwait, the official criterion used for diagnosing and classifying diabetes mellitus is the WHO criterion,[23] and so that was used in the present study.

Ideally, hyperinsulinemia is defined if insulin level exceeds the normal value according to the pubertal stage, due to the impact of physiological insulin resistance of puberty.[24] However, Tanner staging was not assessed during the clinical examination in the present study for social and cultural reasons. Thus, standard values of normal, borderline, and

high fasting insulin levels proposed by the American Heart Association scientific statement were chosen.[25]

HOMA-IR is a proxy for insulin resistance and is widely used in clinical settings and research, with high reliability in determining insulin resistance.[20] There is still a debate about the appropriate cutoff point for HOMA-IR, with proposed values of ≥2.5,[26,27] ≥1.77,[28] and >3.16.[20] Keskin et al[20] found that HOMA-IR was the most sensitive and most specific of three proxies for defining insulin resistance, and the cutoff point for insulin resistance diagnosis based on HOMA-IR was 3.16,[20] so that definition was used in the present study.

Assessment of lipid profile for the participants included fasting TG, fasting cholesterol, fasting LDL, and fasting HDL. Jolliffe and Janssen[29] developed age- and sex-specific percentiles for lipoproteins and cholesterol, starting from age 12 years to age 20 years. However, our participants were aged 10–14 years, and it was not possible to use these lipoprotein percentiles for the whole sample. Therefore, the reference values for these parameters were taken from the National Cholesterol Education Program, with fixed cutoff points for normal, borderline, and high values regardless of sex and age.[30]

Liver function tests were obtained in all participants and included ALT, AST, and GGT. The upper limit for ALT and AST in adults differs between populations, and differences exist between males and females.[31] However, in studies examining the prevalence of abnormal ALT, AST, and GGT in adolescents, the most commonly used cutoff points were >40 U/L, >40 U/L, and >35 U/L, respectively.[15,32,33] Therefore, these were the values that we used as cutoff points in our study.

Markers of inflammation were assessed in all participants, including CRP.[34] Generally, normal and abnormal levels of CRP were developed for the adult population,[34,35] and some studies found that the normal range in healthy adults was from 0.08 mg/L to 6.1 mg/L.[36] Our study used the cutoff points set by the American Heart Association and the Centers for Disease Control and Prevention.[34]

The inflammatory cytokine IL-6 has an age-related variability with peak physiological elevation around age 4 years and 15 years in relation to cartilage and bone development.[37] In the literature, precise reference ranges for IL-6 vary greatly depending on the age, weight status, and sex of the participants tested.[37–39] In the present study, we used the reference range of the control group (healthy controls n=37) from a study by Makni et al[40] (>3.9 pg/mL).

Inflammatory plasma soluble adhesion molecules (ICAM) were also measured in all of the participants.[41] The literature shows that ICAM values are age related, and when applying the cutoff point for our study we chose a study by Andrys et al[42] to establish reference range for serum soluble adhesion molecules in healthy children and adolescents aged 6–15 years, defined by values between the fifth and 95th percentiles for each inflammatory marker. The normal cutoff range for those aged 6–10 years was 206.8–486.8 ng/mL, and for those aged 11–15 years was 184.1–355.0 ng/mL.[42]

The anti-inflammatory adipokine adiponectin was measured in all participants in the fasting state. It is normally present in plasma concentrations of 2–20 μg/mL.[43] Most studies comparing adiponectin concentration in obese adolescents with its concentration in healthy controls referred to "low levels" when adiponectin concentration was <5 μg/mL, as compared with its concentration in healthy control subjects at >10 μg/mL.[44–46] Therefore, in the present study, we used the same cutoff points.

Hypertension was defined as a systolic and or diastolic blood pressure ≥95th percentile for age, sex, and height, measured on three separate occasions.[47] Metabolic syndrome (MetS) was defined according to the International Diabetes Federation (IDF) definition[48] and the Third Adult Treatment Panel (ATP III) definition.[49] Participants were classified as having MetS if they had a waist circumference ≥90th percentile plus two or more of the following criteria according to the IDF definition: TG ≥1.7 mmol/L, HDL <1.03 mmol/L, blood pressure ≥130/85 mmHg, and FBG ≥5.6 mmol/L. Classification of MetS according to the ATP III definition was based on the presence of three or more of the following criteria: waist circumference ≥90th percentile, TG ≥1.24 mmol/L, HDL ≤1.03 mmol/L, blood pressure ≥90th percentile, and FBG ≥6.1 mmol/L.

Results

Characteristics of study participants

Table 1 shows the mean and standard deviation (SD) of all measured parameters for the participants (n=80). The mean age was 12.3 years (SD 1.1 years).

Prevalence of cardiometabolic risk factors

Twenty-six out of the 80 participants (32.5%) had systolic and/or diastolic blood pressure ≥95th percentile for age, sex, and height. Hyperglycemia and hyperinsulinemia were present in 2.5% (two of 80) and 43.8% (35/80) of participants, respectively. Insulin resistance as defined by HOMA-IR value >3.16[20] was found in 67.5% (54/80) of participants. Out of the 80 participants, 27.5% (22/80) had a high TG level, 33.8% (27/80) had a high total cholesterol level, 20% (16/80) had a

Table 1 Descriptive parameters of the adolescents according to sex, mean (standard deviation)

Variables	All participants (n=80)	Boys (n=40)	Girls (n=40)	Number of participants with abnormality (%)	
				Borderline	High
Age, years	12.3 (1.1)	12.4 (1.2)	12.3 (1.1)	na	na
BMI Z-score	2.2 (0.3)	2.2 (0.3)	2.2 (0.3)	na	na
Waist circumference, cm	93.3 (12.2)	96.6 (12.4)	90.0 (11.2)		
Systolic blood pressure, mmHg	122 (11)	125 (11)	119 (9)	na	24 (30.0%)
Diastolic blood pressure, mmHg	77 (8)	78 (8)	77 (7)	na	14 (17.5)
Total cholesterol, mmol/L	4.7 (0.9)	4.7 (1.0)	4.7 (0.8)	25 (31.5%)	27 (33.8%)
LDL, mmol/L	3.0 (0.8)	3.0 (0.9)	3.0 (0.7)	20 (25%)	28 (35.0%)
TG, mmol/L	1.3 (0.5)	1.3 (0.5)	1.3 (0.5)	26 (32.5%)	22 (27.5%)
HDL, mmol/L	1.1 (0.2)	1.1 (0.2)	1.1 (0.3)	60 (75%) low	16 (20.0%)
FBG, mmol/L	4.7 (0.8)	4.8 (0.9)	4.5 (0.6)	na	2 (2.5%)
Fasting insulin, μU/L	26.7 (23.8)	26.4 (25.8)	27.0 (22.0)	21 (26.5%)	35 (43.8%)
HOMA-IR	6.0 (7.3)	6.4 (9.2)	5.5 (5.0)	na	54 (67.5%)
ALT, U/L	34.2 (23.6)	42.2 (21.3)	26.1 (23.4)	na	21 (26.3%)
AST, U/L	58.1 (19.3)	63.3 (15.6)	52.8 (21.4)	na	71 (88.8%)
GGT, U/L	27.0 (12.6)	31.4 (13.9)	22.7 (9.6)	na	14 (17.5%)
CRP, mg/L	4.2 (5.1)	5.0 (4.6)	3.5 (5.5)	31 (38.5%)	34 (42.5%)
IL-6, pg/mL	2.0 (1.8)	1.9 (1.5)	2.0 (2.1)	na	6 (7.5%)
ICAM, ng/mL	461.3 (158.5)	493.2 (158.0)	429.4 (154.6)	na	53 (66.3%)
Adiponectin, ng/mL	50.7 (25.0)	47.0 (21.5)	54.4 (27.9)	na	

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; CRP, C-reactive protein; FBG, fasting blood glucose; GGT, gamma glutamyltransferase; HDL, high-density lipoprotein; HOMA-IR, insulin resistance by homeostasis model assessment; ICAM, intracellular adhesion molecule; IL-6, interleukin-6; LDL, low-density lipoprotein; na, not applicable; TG, triglycerides.

low HDL level, and 35% had a high LDL level. Liver function tests showed high ALT in 26.3% (21/80) of participants, high AST in 88.8% (71/80) of participants, and high GGT level in 17.5% (14/80) of participants. CRP level was high in 42.5% (34/80) of participants, IL-6 level was high in 7.5% (six of 80) of participants, ICAM level was high in 66.3% (53/80) of participants, and adiponectin level was normal in all participants.

Table 2 shows the results of waist circumference, TG, HDL, FBG, systolic blood pressure, and diastolic blood pressure measurements using IDF and ATP III criteria.

Table 2 Metabolic syndrome prevalence using IDF and ATP III criteria in the participants

Anthropometric and biochemical variables	Mean (standard deviation)	IDF	ATP III
Waist circumference (cm)	93.3 (12.2)	66 (82.5%)	66 (82.5%)
TG (mmol/L)	1.3 (0.5)	12 (15%)	37 (46.5%)
HDL (mmol/L)	1.1 (0.2)	26 (32.5)	26 (32.5%)
FBG (mmol/L)	4.7 (0.8)	4 (5%)	2 (2.5%)
Systolic blood pressure	122 (11)	9 (11.5%)	11 (13.5%)
Diastolic blood pressure	77 (8)		
Metabolic syndrome prevalence		17 (21.3%)	24 (30%)

Abbreviations: ATP III, Third Adult Treatment Panel; FBG, fasting blood glucose; HDL, high-density lipoprotein; IDF, International Diabetes Federation; TG, triglycerides.

Seventeen of the 80 participants (21.3%) met the diagnosis of MetS by the IDF definition and 24 of the 80 participants (30%) met the diagnosis of MetS by the ATP III definition.

Discussion

The current study is the first to estimate the prevalence of cardiometabolic risk factors and MetS in a group of obese Kuwaiti adolescents. The main finding of this study was the high prevalence of multiple cardiometabolic risk factors. Out of the 16 risk factors measured, eight were high in ≥30% of the participants (Table 1). The cardiometabolic risk factors with the highest prevalence of abnormal values included AST (88.7% of the sample), HOMA-IR (67.5% of the sample), ICAM (66.5% of the sample), fasting insulin (43.5% of the sample), CRP (42.5% of the sample), LDL (35.0% of the sample), cholesterol (33.5% of the sample), and systolic blood pressure (30.0% of the sample); 96.3% (77/80) of participants had at least one cardiometabolic risk factor as well as obesity.

As mentioned previously, participants of this study were recruited from the baseline stage of a randomized controlled trial of an office-based treatment trial for adolescent obesity in Kuwait (NATTO). One of the findings of the NATTO was poor engagement with treatment, as evidenced by the poor attendance of families in both the intervention and control arms of the trial.[18] Therefore, findings from the present study might have been useful to demonstrate to the adolescents and

their families that their obesity was a medical problem, and so possibly persuade them to engage more with treatment. Moreover, all of the measured parameters in the present study, except for adiponectin, are readily accessible by physicians working in the Ministry of Health – Kuwait in the clinical setting, so their measurement could be part of any treatment protocol for adolescent obesity in the future.

Risk factors for cardiovascular disease and type 2 diabetes mellitus have extended their roots to reach children and adolescents.[6,7,10,50–54] In a study from Iran[55] on 5,528 adolescents aged 10–18 years assessing the relationship between multiple cardiometabolic risk factors (total cholesterol, TG, LDL, HDL, blood pressure, and FBG) with BMI, low physical activity, and an unhealthy diet, BMI had the greatest direct effect on total cholesterol, LDL, TG, FBG, and blood pressure and an inverse relationship with HDL, more than that contributed by inactivity and an unhealthy diet. Kelishadi et al[55] called for immediate interventions to tackle pediatric obesity and its associated cardiometabolic risk factors in order to prevent future risk of MetS and chronic noncommunicable diseases in Iran.

Kardas et al[56] compared the levels of cholesterol, LDL, TG, HDL, FBG, blood pressure, vitamin D, and adiponectin between obese (n=63) and nonobese (n=51) Turkish adolescents aged 10–16 years. Obesity was defined as BMI >90th percentile for an age- and sex-specific Turkish reference population. Cholesterol, LDL, TG, FBG, and blood pressure were significantly higher in the obese group compared with the nonobese group. Adiponectin, vitamin D, and HDL were significantly lower in the obese group compared with the nonobese group. Mean adiponectin value for the obese group was 3.3 (±0.89) ng/mL and in the nonobese group the mean value was 6.0 (±1.4) ng/mL.

In the Netherlands, inpatient children and adolescents (n=80, aged between 8 years and 19 years) diagnosed with severe obesity (defined as BMI SDS ≥3 or BMI SDS ≥2.3 with comorbidities according to the growth percentiles of the Fourth Dutch Growth Study) were evaluated for the presence of multiple cardiometabolic risk factors, namely blood pressure, fasting insulin, FBG, HOMA-IR, cholesterol, LDL, TG, HDL, and CRP,[57] as part of an inpatient treatment trial for their obesity. Data showed that 80% of the participants had at least one impaired cardiometabolic risk factor as well as severe obesity. In comparison with our study, 90% of our participants had at least one impairment with regards to the same cardiometabolic risk factors assessed.

In the present study, almost a third of the participants had MetS according to the ATP III definition.[58] In a study done in Kuwait on apparently healthy female adolescents (n=431, age 10–19 years) to assess the prevalence of MetS using the same definitions that we applied to our study, it was found that MetS was present in 9.1% by the ATP III definition and 14.8% had MetS when the IDF definition was used.[59] In Saudi Arabia, the prevalence of MetS using the IDF definition was 18% among 180 obese 9- to 12-year-olds.[60] Also using the IDF definition in Lebanese adolescents, Nasreddine et al[61] found that 21.2% of the 104 obese adolescents (mean age 16±1.3 years) had MetS, 3.8% of the 78 overweight adolescents (mean age 16.4±1.4 years) had MetS, and 1.2% of the 81 healthy weight adolescents (mean age 16.8 years) had MetS. In Iran, according to the ATP III definition, MetS has been found in 3.3% of Iranian adolescents (n=450, age 15–18 years).[62] In a sample of 321 overweight, obese, and extremely obese adolescents from Brazil (obesity defined using the Centers for Disease Control and Prevention 2000 definition,[19] MetS was found in around 18% of the 10- to 16-year-old adolescents using the IDF definition.[63] Similarly, in the US,[64] it was found that >50% of obese children and adolescents (n=439, aged 4–20 years) had MetS according to definitions modified from ATP III and WHO.[24] In summary, global studies suggest that, as in the present study, MetS is relatively common among obese adolescents.

The present study had a number of strengths. Our participants were generally a fairly homogenous group of Kuwaiti adolescents living in Kuwait City and recruited from three State schools who were examined for the presence of cardiometabolic risk factors, including MetS. The use of traditional markers for cardiovascular disease (ie, lipid profile and blood pressure), multiple markers for inflammation (ie, CRP, IL-6, and ICAM), and, for the first time, adiponectin in a sample of Kuwaiti adolescents, assessment of insulin resistance as well as liver function, all add to the novelty of our study.

However, our study had a number of limitations. First, it was not possible to conduct Tanner staging, due to social/cultural and practical reasons. Second, the optimal cutoff to define abnormality for a number of the cardiometabolic risk factors is unclear, but widely used cutoffs were chosen for the present study. Third, no data on changes in cardiometabolic risk factors during obesity treatment were available. Improvements in cardiometabolic risk profile might increase engagement with obesity treatment. Nonetheless, the relatively high prevalence of abnormal values for cardiometabolic risk factors found in the present study could be a useful aid to engage more families into participating in adolescent obesity treatment in future, and might also increase the level of commitment to participation by those who do take part.

Conclusion

The present study suggests that a number of cardiometabolic risk factors and MetS are prevalent in obese Kuwaiti adolescents. This observation might provide impetus to future strategies to treat pediatric obesity and to prevent or delay the appearance of cardiovascular disease and diabetes mellitus in the future adult generation. The observation might also be used to encourage greater engagement with treatment among families.

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Disclosure

The authors report no conflicts of interest in this work.

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