

Review of Literature

The review of literature pertaining to the present study entitled **“Evaluation of a Functional Food Supplement on Body composition of Obese Young Adults and Influence of a selected PPAR Gamma Gene Polymorphism on its Outcome”** is presented under the following headings.

- A. Prevalence of obesity
- B. Measures of obesity and body composition analysis
- C. Risk factors of obesity
- D. Importance of physical activity
- E. Role of functional foods
- F. Genetics of obesity with reference to PPAR gamma polymorphism

A. PREVALENCE OF OBESITY

Obesity is described as a global pandemic and is the most widespread metabolic disorder in several countries. (Marie *et al.*, 2014, Constantine *et al.*, 2008) According to WHO, overweight and obesity are defined as abnormal or excessive fat (adipose tissue) accumulation which occurs as a result of an energy imbalance either due to increased energy intake or decreased energy output or a combination of both (WHO, 2015). Since obesity is a complex and multifactorial disorder, a single causative factor cannot be pointed out. Obesity is a consequence of complex interactions between genetic, social, environmental and behavioral factors. (Constantine *et al.*, 2008, Seagel *et al.*, 2009). It is a serious chronic disease and is a predisposition to complicating conditions like cardiovascular diseases, type 2 diabetes mellitus, certain cancers, asthma, sleep apnoea and osteoarthritis. Obesity is often accompanied by inflammatory responses. Visceral obesity is linked to an increased risk of insulin resistance, cardiovascular events and oxidative stress as a result of these inflammatory

processes. C -reactive protein is an inflammatory marker and its elevated level is an independent predictor of endothelial dysfunction and cardiovascular diseases. Obesity not only has clinical effects but also causes social stigmatization. Along with this, obese individuals also suffer from psychosocial and physical functional impairment. This deteriorates the quality of the life of individuals.

1. Global Prevalence

Worldwide obesity has more than doubled since 1980. In 2014, more than 1.9 billion adults, 18 years and older, were overweight. Of these over 600 million were obese. 39% of adults aged 18 years and over were overweight in 2014, and 13% were obese. Most of the world's population live in countries where overweight and obesity kills more people than underweight (WHO Fact sheet, 2016).

Owing to the rising urbanization and industrialization, worldwide obesity has nearly doubled since 1980, in 1980: 857 million individuals were overweight and obese which increased to 1.9 billion by 2014. Of this, 600 million were obese.

WHO global estimates from 2014 revealed that overall 39 per cent of world's adult population were overweight and 13 per cent were obese. Overweight and obesity are no longer a problem of high income countries but are also on a rise in low and middle income countries. (WHO, 2015).

Globally, there is a rising prevalence of overweight and obesity in both developing and developed countries (Haidar and Cosman, 2011), The rate of obesity has tripled in developing countries over the past 20 years as they rapidly become more urbanized, with increased consumption of high calorie foods and adoption of a more sedentary lifestyle (Haidar and Cosman, 2011), (Popkin *et al*., 2012). Some studies observed that first year university students have significant weight gain (Vella- Zarb and Elgar, 2009), followed by ongoing slow but steady increase in weight (Gores, 2008). India and china together accounted for 15 per cent of world's adult obesity population with 30 million and 46 million obese individuals respectively.

Studies among university students in developing countries show high prevalence of overweight and obesity: Africa (Nigeria: 10% [Nwachukwu et al.,2010]; Egypt: 25.3%–59.4% [Abolfotouh et al., 2007 and Bakr et al .,2002], South Africa: 10.8%–24% [Cilliers et al .,2006 and Bodiba et al., 2009]; Asia (Bangladesh: 20.8% (Sultana et al.,2007); China: 2.9%–14.3% (Jingya et al.,2013); Malaysia: 20%–30.1% [Gopalakrishnan et al.,2012], Thailand: 31% [Banwell et al.,2009], Pakistan: 13%–52.6% [. Chaudhry et al., 2012], and India: 11%–37.5% [Bhongir et al .,2011; Latin America (Colombia: 12.4%–16.7% [Vargas et al .,2008]; Mexico: 31.6% [Trujillo-Hernández et al., 2010], the Middle and Near East (Saudi females: 47.9% [Al Qauhiz , 2010]).

2. Prevalence of Obesity in India

India, with 1.2 billion people is the second most populous country in the world and is currently experiencing rapid epidemiological transition. Under nutrition due to poverty which dominated in the past, is being rapidly replaced by obesity associated with affluence (Mohan and Deepa, 2006). Industrialization and urbanization also contribute to increased prevalence of obesity. Studies from different parts of India have provided evidence of the rising prevalence of obesity (Mohan and Deepa, 2006; Bhardwaj et al., 2011, Deepa et al., 2009 and Misra and Khurana,2008).

The National Family Health Survey-3 (NFHS-3,2006) also reported that in India, obesity (BMI \geq 25 kg/m²) was more prevalent in the urban areas and in higher socio-economic groups compared to the rural areas, especially among women (Men- urban: 15.9 vs. rural: 5.6%; Women- urban: 23.5 vs. rural: 7.2%). According to the NFHS-3 data, in the three states studied, the percentage of women who were obese (BMI \geq 25 kg/ m²) was highest in Tamil Nadu (24.4%), followed by Maharashtra (18.1%) and Jharkhand (5.9%) and a similar order was reported among men in the three states with 19.8, 15.9 and 5.3 per cent being obese respectively(IIPS,2007)

Asian Indians have a greater predisposition to abdominal obesity and accumulation of visceral fat and this has been termed as “Asian Indian phenotype (Joshi, 2003 and Deepa *et al.*, 2006). In a study conducted in urban north India (New Delhi), the overall prevalence of generalized obesity was 50.1 per cent, while that of abdominal obesity was 68.9 per cent (Bhardwaj *et al.*, 2011). The Chennai Urban Rural Epidemiology Study (CURES) conducted in Chennai city in Tamil Nadu reported age standardized prevalence of generalized obesity to be 45.9 per cent, while that of abdominal obesity was 46.6 per cent. Isolated generalized obesity was found in 9.1 per cent while isolated abdominal obesity was reported in 9.7 per cent (Deepa *et al.*, 2009).

In India, urbanization is caused by urban expansion into peripheral areas and internal migration from rural to urban areas, largely for economic reasons. Urbanization increases the risk of obesity and diabetes among people who have had divergent early life experiences, particularly in developing countries (McKay *et al.*, 2003). While the trends of increased risk of obesity and diabetes among both international south Asian migrants is well documented (Barnett *et al.*, 2006 and Landman and Cruickshank, 2001).

Epidemiologists project a gloomy picture of the health of young people. During the past two decades, a significant increase in obesity and obesity-related disorders such as type 2 diabetes, hypertension, and dyslipidemia has occurred among people in their teens and 20s (U.S. Department of Health and Human Services. ,2001 and www.cdc.gov).

In countries like India, the rise in obesity prevalence could be attributed to the increasing urbanization, use of mechanized transport, increasing availability of processed and fast foods, increased television viewing, adoption of less physically active lifestyles and consumption of more “energy-dense, nutrient-poor” diets (WHO,2003, Bell *et al.*,2002 and Misra *et al.*, 2010) . This is exemplified by the higher prevalence of both general obesity and abdominal obesity in the urban population where the above factors are more common.

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Nearly 70 per cent of India’s population resides in rural areas. Even a small increase in prevalence of obesity in rural areas could lead to a huge increase in the number of obese individuals in India. Ramachandran *et al* (1992) evident in study that there was a marked increase in BMI values in the rural areas of south India. The increase in prevalence of obesity among the rural population may be due to rapid changes in lifestyle in rural areas.

Many studies in India have reported higher prevalence of obesity among women (Singh *et al.*, 2007). In a study conducted in four urban and five rural locations in India among women aged 35-70 yr, the age-adjusted prevalence of obesity (BMI \geq 25 kg/m²) in urban and rural areas was 45.6 and 22.5 per cent, respectively (Pandey *et al.*, 2013). The NFHS-3 data which studied urban and rural residents (all women aged 15-49 and all men aged 15-54) in 28 states of India and the National Capital Territory of Delhi during the year 2005-2006, also showed a higher prevalence of overweight (BMI \geq 25-29.9 kg/m²) and obesity (BMI \geq 30 kg/m²) among females than males in all the states of India (IIPS, 2007).

3.Prevalence of Obesity in Tamil Nadu

NFHS - 4 (2016) indicates that 30.6 and 36.2 per cent of urban male and females are overweight or obese while in the rural it was reported as 30.6 and 25.6 per cent in male and female respectively.

The prevalence of obesity observed in women in the three states included in our study was similar to that observed in NFHS-3, with the highest prevalence in Tamil Nadu (INDIAB: 24.6 vs. NFHS-3: 20.9%), followed by Maharashtra (INDIAB: 16.6 vs. NFHS-3: 14.5%) and Jharkhand (INDIAB: 11.8 vs. NFHS-3: 5.4%). The prevalence of obesity among Indian women has increased from 10.6 per cent (NFHS-2 in 1998-1999) to 12.6 per cent (NFHS-3 in 2005-2006), *i.e.* an increase by 24.52 per cent in a 7 year period (Garg *et al.*, 2010)

The metabolic syndrome, which is defined by a cluster of risk factors that include obesity, hypertension, hyperglycemia, and dyslipidemia, identifies individuals at increased risk of type 2 diabetes and cardiovascular disorders (Haffner *et al.*, 1992 and Isomaa *et al.*, 2001). As obesity has become more common, the prevalence of the metabolic syndrome has increased, and these trends are likely to continue (National Task Force on the Prevention and Treatment of Obesity, 2000, Ford *et al.*, 2004 and Ford *et al.*, 2002).

B. MEASURES OF OBESITY

Obesity has become one of the major contributors to the global burden of diseases, increasing the risk of metabolic syndrome and risk of morbidity and mortality from cardiovascular diseases, type 2 diabetes and some cancers. The risk functions for obesity, (defined as the quantitative relation between degree of obesity throughout its range and the risk of health problems) have been used to define 'obesity' as an excess storage of fat in the body to such an extent that it causes health problem leading to increased mortality. BMI, waist circumferences (WC), waist hip ratio (WHR) have been used for assessment of nutritional status and risk factors of metabolic syndrome.

1. Body Mass Index

BMI does not necessarily describe the same degree of fatness in different populations, partly because of differences in body proportions. Asians and Indians have a more centralized distribution of body fat for a given level of BMI compared to people of European descent (Deurenberg-Yap *et al.*, 2000, Ko *et*

al., 2000). BMI is a simple index of weight/for/ height that is commonly used to classify, overweight and obesity in adult. It is defined as the weight in kilograms divided by the square of the height in meters. (kg/m²).

WHO classifies BMI over 25 as overweight and BMI over 30 as obese for Asian population, additional trigger points for public health action were identified as 23kg/m² or higher, representing increased risk and 25.5kg/m² or higher as high risk.

Among Asians and Indians morbidity and mortality occur at a lower BMI, and it is proposed that the BMI cut-offs for overweight and obesity in these populations be lowered to >23 and >25 respectively (WHO, 2000). BMI is widely used to assess obesity in populations and influenced by age, gender and ethnicity makes it a less useful measure when used alone in individuals, at least where BMI is less than 30(Frankenfield *et al.*, 2001). Combining BMI with a measure of fat distribution may help overcome some of the problems of using BMI alone in the clinical situation.

BMI is an acceptable approximation of total body fat at the population level and can be used to estimate the relative risk of disease in most people. However, it is not always an accurate predictor of body fat or fat distribution, particularly in muscular individuals, because of differences in body-fat proportions and distribution.

2.Waist circumference:

BMI does not distinguish between mass due to body fat and mass due to muscular physique. It also does not take account of the distribution of fat. It has therefore been postulated that waist circumference may be a better measure than BMI or waist to hip ratio (WHR) to identify those with a health risk from being overweight. For south Asians the cut-off for waist circumference is >90cm for men and >80cm for women.

A raised waist circumference has been taken to be greater than 102cm in men and greater than 88cm in women, in accordance with the definition of abdominal obesity used by the National Institutes of Health (USA) ATP (Adult Treatment Panel) III (National Institute of Health,2001). These levels identified people at risk of the metabolic syndrome. Waist circumference and waist -to-hip ratio are strongly predictive in young and middle – aged adults compared to older people and those with low BMI: waist circumference alone could rep-lace waist hip ratio and BMI as single risk factor for all-cause mortality.

3.Conicity Index:

The Conicity Index was developed as an indicator of abdominal obesity, and it expresses an individual's waist circumference relative to the circumference of a cylinder generated from the subject's height and weight, assuming a constant for body density. The conicity index was calculated as follows:

$$\text{Coincidity Index} = \text{waist circumference} / (0.109 \times \text{square root of weight} / \text{height})$$

where waist circumference and height were measured in meters and weight was measured in kg. To measure central obesity, various indices have been suggested; among them, waist circumference (WC), waistto-hip ratio (WHR), and waist-to-height ratio (WHtR) are regarded as the most popular indices that are widely applied in clinical settings. More recent indices, abdominalvolume index (AVI) and conicity index (CI), which are calculated on simple data such as weight, height, WC, and hip circumference (HC), have also been introduced (Guerrero-Romero *et al.* , 2003).

BMI is the most commonly used and simple measure of body size, especially for estimating the frequency of obesity in large epidemiological studies (Colditz *et al.*, 1995). It has been shown that intra-abdominal fat has a stronger relationship with risk of obesity-related morbidity than with overall adiposity (Hoet *al.*, 2001). Therefore WHR and WC measurements can be used as valid alternatives to BMI for the evaluation of intra-abdominal mass and total fat (Dalton *et al.*, 2003). A study by Huang and co-workers showed that WHR and

WC measurements were strongly associated with incidence of coronary heart disease, independent of BMI (Huang *et al.*, 1997).

Body mass index (BMI; in kg/m²) is widely used to measure overweight and obesity, and the WHO and the National Institutes of Health (NIH) use similar BMI cutoffs to define overweight (BMI >25) and obesity (BMI >30). It is now accepted that the distribution of body fat is an important determinant of metabolic abnormalities, possibly more so than the degree of excess weight as measured by BMI. In particular, intra abdominal obesity or visceral fat is strongly associated with metabolic disturbances and insulin resistance. Hence, in view of abovementioned observation, a study designed to evaluate abdominal volume index (AVI) and Conicity index (CI), which reflect adipose tissue in viscera and abdominal organs, will be a useful criterion for early identification of metabolic abnormalities and help in taking measures of further progress in the state of condition. .

4.Body composition Analysis

Besides these waists to hip ratio and body composition are also used to identify obesity. A higher body fat is strongly associated with increased risk of metabolic syndrome, thus while treating obesity the aim should be to lose body fat and maintain, fat free mass/lean body mass.(WHO, 2008), Misra *et al.*, 2009.) Body composition analysis is based on Bioelectrical Impedance Analysis (BIA). Bio impedance devices that pass a small, alternating electric current through the body, and the resistance to that current indicates the amount of water in the body. This is, in turn, related to the amount of lean tissue in the body and the opposition of the flow is measured.

There are several compartment models for the human body. They range from a simple two compartment model to a four compartment model. The goal in body composition is to measure one of these compartments and assume that the relationship between the compartments is constant to estimate another compartment. In the clinical setting the fat compartment is most commonly measured because excess body fat is associated with modern chronic disease.

The four-compartmental (4C) is more robust with respect to inter-individual variability in the composition of FFM. This model divides the FFM into measured water and mineral mass, and only assumes the density of the remaining components of the FFM (protein, DNA, glycogen, etc), and is, therefore, the best reference method, given the primary measurements available

Bioelectrical impedance analysis (BIA) is a widely used method for estimating body composition. The technology is relatively simple, quick, and noninvasive. BIA is currently used in diverse settings, including private clinicians' offices, health clubs, and hospitals, and across a spectrum of ages, body weights, and disease states. Despite a general public perception that BIA measures "body fat," the technology actually determines the electrical impedance of body tissues, which provides an estimate of total body water (TBW). Using values of TBW derived from BIA, one can then estimate fat-free mass (FFM) and body fat (adiposity).

In addition to its use in estimating adiposity, BIA is beginning to be used in the estimation of body cell mass and TBW in a variety of clinical conditions. BIA measures the opposition of body tissues to the flow of a small (less than 1 mA) alternating current. Impedance is a function of two components (vectors): the resistance of the tissues themselves, and the additional opposition (reactance) due to the capacitance of membranes, tissue interfaces, and nonionic tissues. The measured resistance is approximately equivalent to that of muscle tissue. Impedance measures vary with the frequency of the current used (typically 50 kHz, when a single frequency is used). Applications of BIA increasingly use multifrequency measurements, or a frequency spectrum, to evaluate differences in body composition caused by clinical and nutritional status.

C. RISK FACTORS OF OBESITY

1. Familial and Ethnic Factors

Environmental factors of a familial nature including ethnic food preferences, eating patterns, dietary composition differences (e.g., high-fat diets), and activity levels, play a role in the etiology of obesity. Studies of energy

expenditure in individuals and families show that differences are greater between families vs within families (Bogardus, 1986). This may be the result of genetic factors affecting energy metabolism, but could also be owing to learned patterns of activity. Different ethnic groups demonstrate marked differences in the character and amounts of foods eaten. Factors that may influence total calorie intake include the frequency and timing of eating and the use of spices, oils and fats, and preferred food sources (e.g., rice, wheat)

2. Diet Composition and Eating Patterns:

In considering factors that may have played a role in the epidemic of obesity, increases in food intake are high. World are becoming more affluent and able to afford more food and more commercially prepared foods, which tend to have a higher energy density. Ease of access to food has increased with more restaurants, especially fast food restaurants that have quite inexpensive, high-fat, high-calorie foods as their staples. Portion sizes have increased since the 1980s. With more leisure-time activity, especially watching TV, food intake increases. Excessive calorie intake above daily energy requirements is necessary for the development of obesity, but it is incorrect to assume that simple overeating is responsible for all obesity and there is evidence that the quality of the foods ingested also is important in producing obesity.

In animal studies, diets high in fat produce a greater degree of obesity than those high in carbohydrate (CHO). There are several reasons that increased dietary fat produces obesity. Fat contains more than twice as many calories per gram as protein or CHO. Eating the same volume of food results in much greater energy intake on a high-fat diet than on a low-fat diet. Also, high fat foods are more palatable than low-fat foods. Fat adds a desirable “mouth feel” to foods that animals and humans prefer. Fatty foods are usually low in dietary fiber, are softer, and require less time to chew and swallow than other types of foods. This is particularly true of high-fat desserts. Because there is less processing time for high-fat foods, it is easier to eat larger amounts. Finally, there is evidence that high-fat foods do not produce satiety as well as do high-CHO foods

(Rolls *et al.*, 1994). Experiments in which subjects were fed a high- or low-fat preload before a meal showed that total energy intake was greater with the high-fat preload. The subjects did not perceive the increased energy of the preload, ate a comparably sized meal, and thus obtained a greater total energy intake.

3. Emotional Stress:

Several types of stress may contribute to obesity; perhaps the most studied of which is emotional stress. Depression is associated with weight gain in about 10 to 20% of cases. On an anecdotal basis, many patients report that the onset of obesity occurred with some major emotionally stressful event in their lives. However, it is difficult to identify a suitable control group for such events. Multiple studies have shown that surgery, such as tonsillectomy, is associated with an increased incidence of obesity compared to unoperated controls in the period after surgery (Camilleri *et al.*, 1995)

4. Trauma :

Central nervous system damage Injury to selected areas of the central nervous system (CNS) from accidents or neoplasms is known to cause obesity in a small number of patients (Bray, 1984). Probably the most common type of injury is head trauma from automobile accidents. Pituitary or hypothalamic tumors are the most common types of neoplasms associated with the onset of obesity (Bray *et al.*, 1984).

5. Drugs:

It is not well recognized, but numerous drugs may produce an increase in food intake or body weight. Glucocorticoids produce fat gain, particularly truncal adiposity, in a high percentage of users. Insulin and oral hypoglycemics (sulfonylureas and thiazolidinediones) promote weight and adipose tissue gain in diabetics. Phenothiazines, a typical antipsychotic agent, and some antidepressants, such as tricyclics and selective serotonin reuptake inhibitors, may produce weight gain. Cyproheptadine and valproic acid also have been implicated in the etiology of obesity in some patients. Finally, (alpha or beta in symbol)-adrenergic antagonists such as propranolol are postulated to reduce

Sour sympathetic nervous system activity and lead to weight gain or difficulty in losing weight.

D .IMPORTANCE OF PHYSICAL ACTIVITY

“Physical activity” refers to any body movement that burns calories, whether it’s for work or play, daily chores, or the daily commute. “Exercise,” a subcategory of physical activity, refers to -planned, structured, and repetitive-activities aimed at improving physical fitness and health.

- Physical activity increases people’s total energy expenditure, which can help them stay in energy balance or even lose weight, as long as they don’t eat more to compensate for the extra calories they burn.
- Physical activity decreases fat around the waist and total body fat, slowing the development of abdominal obesity.
- Weight lifting, push-ups, and other muscle-strengthening activities build muscle mass, increasing the energy that the body burns throughout the day-even when it’s at rest-and making it easier to control weight.
- Physical activity reduces depression and anxiety, and this mood boost may motivate people to stick with their exercise regimens over time.

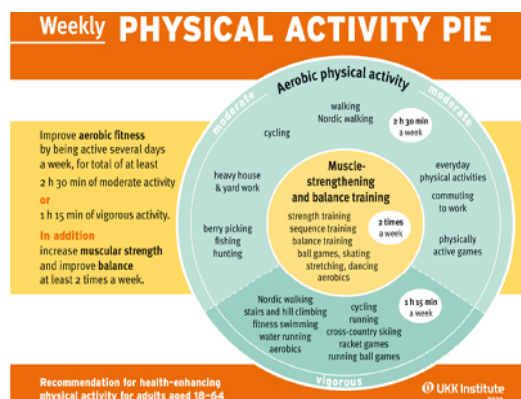


Figure 1

Recomendation for physical activity

(Source : http://www.ukkinstituutti.fi/en/products/physical_activity_pie)

E. ROLE OF DIET AND FUNCTIONAL FOODS

A change in the diet structure is needed to keep up with the on-going nutrition transition and also to combat the ever rising incidence of coronary heart disease, diabetes and obesity. Healthy eating may be best achieved with a plant-based diet, which encourages whole plant based foods and discourages meats, dairy products and eggs as well as all refined and processed food. (TUSO *et al.*, 2013). Whole grain oat appears to be most effective whole grain for lowering cholesterol (Hollaender *et al.*, 2015). Brans derived from rice, wheat, oat, barley, shorgum, millet, rye and maize have been characterized to possess a wealth of health promoting ingredients. They have been validated to impart anti-lipidaemic, anti-arthrogenic, anti-hypertensive and satiety and alleviate cardiovascular complication (Patel, 2015).

A reduction of 500-1000Kcal/d is usually the first recommendation in the treatment of obesity. A daily reduction by 600Kcal would result in weight loss by 0.5kg/week. However, energy restriction needs to be individualised. Reduction in caloric intake could either focus only on calorie count and /or macro nutrient proportion along with changes in meal frequency, portion sizes and meal timing. The following diets are most commonly recommended:

- Hypocaloric balanced diets – these diets provide ~1200 Kcal/day or more
- Low calorie diet (LCD) : these diets constitute about 800-1200 Kcal/day
- Very low calorie diet (VLCD): these provide less than 800 Kcal/day and are typically liquid formulation. VLCD should not be used for long-term as they are associated with micro nutrient deficiencies and should be supervised by a health professional. (Constantine *et al.*, 2008, Seagle *et al.*, 2009).

Taking this trend of nutrition transition towards the functional food concepts requires huge momentum and dissemination of the same in relation to their health benefits. Functional foods have the potential to be an increasingly important component of healthy life style and to be beneficial for public health as well as provide insight for wider product range for the food industry.

Functional food components are potentially beneficial components found naturally in foods or added to them as functional ingredients, and include carotenoids, dietary fiber, fatty acids, flavonoids, isothiocyanates, phenolic acids, plant stanols and sterols, polyols, prebiotics and probiotics, phytoestrogens, soy protein, vitamins and minerals.

1. Dietary fibers

Dietary fibers include cellulose, hemicellulose, polyfructoses, galactooligosaccharides, gums, mucilages, pectins, lignin and resistant starches, and are classically divided into soluble or insoluble. More recently, some are proposing the use of the terms "viscous" and "fermentability" in place of soluble and insoluble to describe the functions and health benefits of dietary fiber. Both soluble and insoluble fibers pass through the stomach and small intestine undigested, but when they reach the large intestine they are fermented by colonic bacteria in different extensions. As a result of the fermentation process short chain fatty acids are produced, providing the important health benefits of fiber.

Dietary fibers refer to non-digestible and non-absorbable part of plant food with complete or partial fermentation in the colon that result in production of short chain fatty acids. (SCFA). These includes insoluble fibres such as wheat bran and soluble fibres from oats, fruits and oligosaccharide (Huaidong *et al.*, 2010, David *et al.*, 2014). high fibres diets have been associate with beneficial effects on body weight by reducing energy intake and co-morbid conditions(Huaidong *et al.*, 2010, Ellen *et al.*, 2014) various physiological benefits of fibres have been evaluated for its effect on weight control, post-prandial glucose and hormonal responses, gastric emptying and intestinal transit time. (David *et al.*, 2014). Fiber rich diets tend to be more satiety as they slow down gastric emptying by forming viscose gel in the small intestine, which reduces absorption of nutrients, there by prolonging satiety reduces post prandial glucose and over a long term improves insulin sensitivity

Functional fiber is something that manufacturers deliberately add to food products to provide similar health benefits to those of dietary fiber, without adding

significant calories. Some examples of functional fibers are cellulose, maltodextran, polydextrose, and inulin, and these are isolated from foods where they occur naturally. The consumption of dietary and functional fibers has many potential health benefits, namely the ability to lower the incidence of constipation (Castillejo, 2006) and irritable bowel syndrome (Malhotra,2004), lower cholesterol and diminish the incidence of coronary and cardiovascular heart diseases (Romero, 2002; van Rosendaal, 2004), prevent obesity (Murakami, 2007) and diabetes (Hannan, 2007), avoid colon cancer (Wakai,2007) and increase survival in breast cancer (McEligot, 2006).

2.Soy protein

Soy protein, a major constituent of soybeans, is unique among the plant-based proteins and is considered a complete protein because it contains large amounts of all the essential amino acids, besides many other macronutrients with a nutritional value. It is associated with isoflavones, which have many potentially health benefits, and the replacement of animal based foods by soy proteins is furthermore advantageous, since those contain much higher amounts of fat, and particularly saturated fat.

According to the review by Montgomery (2003), soy protein products offer benefits to women in various life stages, including improved diet and cardiovascular status, prevention of certain types of cancer, health improvement following menopause and obesity prevention. Soy protein showed some chemopreventive activity as reported by Xiao *et al* (2005). The consumption of soy protein helps reducing body weight and fat mass as well as lowering plasma cholesterol and triglycerides (Velasquez, 2007). Since high levels of total cholesterol and LDL cholesterol constitute important risk factors for coronary heart disease, one of the most common and serious forms of cardiovascular disease, soy protein was indicated by many studies as a health promoting factor for coronary heart disease, which lead the Food and Drug Administration (FDA) to approve in October 1999 a health claim for soy protein and coronary heart disease (Sacks, 2006).

3. Flax seeds (*Linum usitatissimum*)

Flaxseeds contain approximately 30% dietary fibers of which one third is viscous, and the majority of the flaxseed water-extractable dietary fibers (the mucilage) belong to a group of heterogenic polysaccharides. These are neutral arabinoxylans and highly acidic rhamnose-containing polysaccharides present on the outside of the seed coat, which are characterized as highly viscous (Naran, Chen and Carpita, 2008). There is an unmet need for food additives or dietary supplements that can prevent further weight gain or induce weight loss among obese individuals (Ibrügger *et al.*, 2012). Flaxseeds play a vital role in lowering total and LDL cholesterol levels, reduce postprandial glucose absorption, decrease markers of inflammation and raise serum levels of omega-3 fatty acids. Studies revealed that up to 50g of alpha-linolenic acid flaxseed / per day are palatable, safe and may nutritionally benefit humans by raising n-3 fatty acids in plasma.

4. Defatted soy flour:

Soy is a rich source of protein as well as fat. The fat content was removed in order to prepare the supplement. Soy and its product are known to possess hypotriglyceridic effect and lowers adipocytes. Further studies reveal that there was a significant inverse relation between genistein consumption and markers of metabolic syndrome including weight, BMI, waist circumference and total body fats in human subjects consuming western diet. (Gruen and Silverstein, 2003) the amount of isoflavone in 100gm of variously soy processed ranges from 0.1 to 50mg- soy drink (7mg), unsalted immature cooked boiled soy (14mg), iced soy milk (4mg), soy sauce made from hydrolysed vegetable protein (0.1mg), soy bean chips (50mg). Soy flour as such contains 130 to 200mg of soy isoflavone and defatted soy meal contains 130mg of isoflavone per 100g. (Ungar and Shimoni, 2004).

5. Wheat Bran

Wheat (*Triticum aestivum*) is a leading cereal crop which is mainly utilised for human consumption and livestock feed. A wheat kernel comprises three principal fractions – bran, germ and endosperm. The outer layers are all

parts of the bran. The bran fraction is a by-product of milling and has food (Curti *et al.*, 2013) and nonfood applications (Aprich *et al.*, 2013). WB is rich in minerals, fibre, B vitamins and bioactive compounds which are known to possess health-promoting properties (Reisinger *et al.*, 2013). Arabinoxylan (AX) is a fibre that has a β -D-xylan in wheat bran. It was recently stated that arabinoxylans may reduce postprandial glycemic response by maintaining viscosity in the gut, thereby reducing the risk of developing type II diabetes, but this was obtained from arabinoxylans of wheat endosperm (Bernstein *et al.*, 2013).

Most of the health benefits of WB are associated with but not limited to its dietary fibre content. Water swelling, holding and retention capacities of fibre have been associated with other health functions, viz reduction in plasma cholesterol, laxative ability and reduction in blood glucose (Patel, 2015). Furthermore, fibre help in maintaining positive health in the gut, appetite regulation and prolonged satiety (Oluwatoyin *et al.*, 2015). It has been suggested that the antioxidant phytochemicals found in wheat bran fractions may modulate cellular oxidative status and prevent biologically important molecules such as DNA, proteins and membrane lipids from oxidative damage and consequently play a role in reducing the risk of chronic disease. (zhou *et al.*, 2004). Phenolic antioxidants present in wheat bran have been shown to inhibit LDL oxidation (yu *et al.*, 2005). liyanapathirana and Shahidi (2007) opined that higher antioxidant activity was found in bran fraction.

6.Oats

Although some of the antioxidants in oats are heat labile, most are heat stable; this is an advantage since commercial oat products are often heat treated to inactivate enzymes and are served hot as a cooked cereal. The main component of oat soluble fiber is (1/3)(1/4)- β -D glucan, commonly known as β -glucan. The Food and Drug Administration allows a claim that food products containing oats and that can deliver 3 g β -glucan/d can reduce risk of heart disease. In addition, The Joint Health Claims Initiative in the United Kingdom allows a claim that the inclusion of 3 g oat β -glucan in food products can help reduce blood cholesterol. (Wolever *et al.*, 2010). The US drug and administration

recommends 3g beta glucan per day to reduce heart disease. Consumption of oats is also known to reduce obesity, abdominal fat, and improve lipid profiles as well as liver function.

It remains possible that particular classes of food or individual foods can confer specific benefits. The effects of oats and lipid metabolism are well documented, and there is a growing body of literature to suggest that oats also lower blood pressure or help prevent CVD. Population studies suggest that diets rich in oats or other foods containing soluble fibres are associated with lower level of blood pressure or rates of coronary disease. Oats fibre consumption has been shown to reduce post prandial glucose and insulin concentration, reduction in the insulin concentration may provide the mechanism by which blood pressure could be reduced in response to oats consumption. Oats also contain a varied range of phenolic compounds including ester linked glycerol conjugates ester linked alkyl conjugates ether ester linked glycerides, anthranilic acids and avenathramides. These compounds possess high level of antioxidant activities. Compared with other cereals (wheat, rice, barley, buckwheat, rice), oats contain higher content of protein, and the composition of amino acid is more reasonable.

Nutritional and functional potential in oat are much higher than of other cereal grain, which leads oat to become an excellent source of functional food. Oat lipids are rich in poly unsaturated fatty acids, vitamin E and plant sterols.

F. GENETICS OF OBESITY WITH REFERENCE TO PPAR GAMMA POLYMORPHISM

Nutrigenetics and nutrigenomics are defined as the science of the effect of genetic variation on dietary response and the role of nutrients and bioactive food compounds in gene expression, respectively (Simopoulos, 2010). Nutrigenetics and nutrigenomics hold much promise for providing better nutritional advice to the public generally, genetic subgroups and individuals. Because nutrigenetics and nutrigenomics require a deep understanding of nutrition, genetics and biochemistry and ever new 'omic' technologies, it is often difficult, even for educated professionals, to appreciate their relevance to the practice of preventive

approaches for optimising health, delaying onset of disease and diminishing its severity (Fenech *et al.*, 2011)

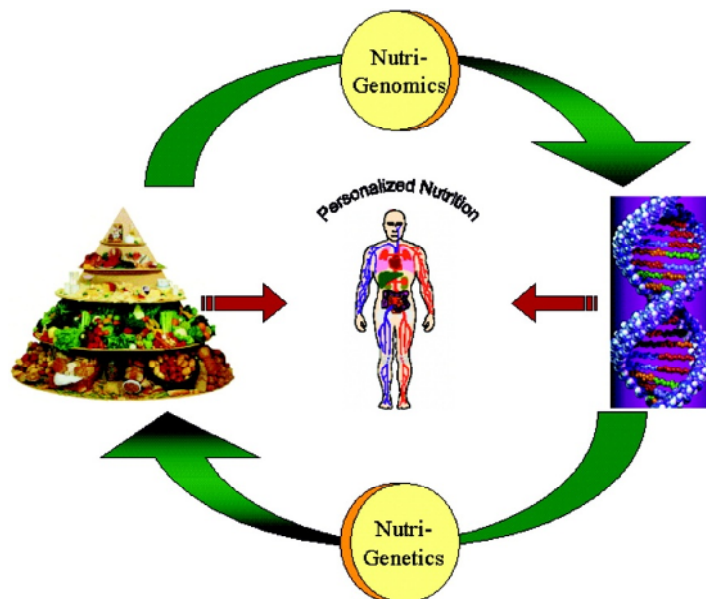


Figure 2
Nutrigenomics and Nutrigenetics
Source: Muller and Kersten, 2003

There are three central factors that underpin nutrigenetics and nutrigenomics as an important science. First there is great diversity in the inherited genome between ethnic groups and individuals which affects nutrient bioavailability and metabolism. Second, people differ greatly in their food/nutrient availability and choices depending on cultural, economical, geo graphical and taste perception differences. Third malnutrition (deficiency or excess) itself can affect gene expression and genome stability; the latter leading to mutations at the gene sequence or chromosomal level which may cause abnormal gene dosage and gene expression leading to adverse phenotypes during the various life stages (Fenech *et al.*, 2011). The ability of diet to affect the flow of genetic information can occur at multiple sites of regulation

Obesity results from interactions between environmental and genetic factors. Despite a relatively high heritability of common, non-syndromic obesity (40–70%), the search for genetic variants contributing to susceptibility has been a challenging task. Genome wide association (GWA) studies have dramatically

changed the pace of detection of common genetic susceptibility variants. To date, more than 40 genetic variants have been associated with obesity and fat distribution. However, since these variants do not fully explain the heritability of obesity, other forms of variation, such as epigenetics marks, must be considered. (Ordovas and Corella, 2004). Genetic variation across the human genome is being recognised as increasingly complex. Single nucleotide polymorphisms (SNPs) are the most common form of sequence variation in the human genome with >10 million SNPs reported in public databases (Thorisson and Stein, 2003)

Common polymorphisms can occur in up to 40–50 per cent of the population. Genetic polymorphisms may either have no consequence or have significant effects on the structure or function of the gene product. Different experimental approaches can be used to identify genetic variants that modify the effects of dietary factors or influence food preferences

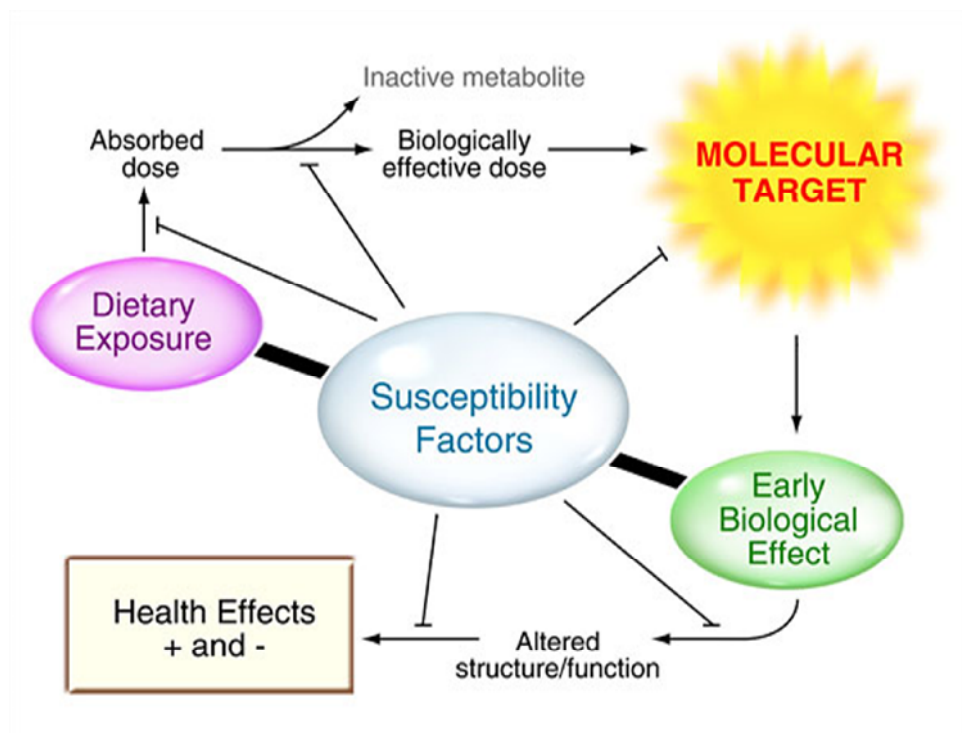


Figure 3

Molecular Targets – susceptibility factors

(Source: Combs *et al*, 2013)

A candidate gene approach is the most common method whereby a gene is selected based on its known or putative function. Depending on the number of SNPs in the gene, and whether any of them have known functional effects, analyses can be conducted using individual SNPs or combinations of SNPs, such as haplotypes

Socio-economic and lifestyle changes are major contributing factors in the development of obesity. It has been proven in many studies that genetics also play a significant role. Obesity is regarded as a multifactorial condition wherein susceptibility is determined by the interplay of genetics and environmental factors. It is generally regarded as a complex genetic disorder

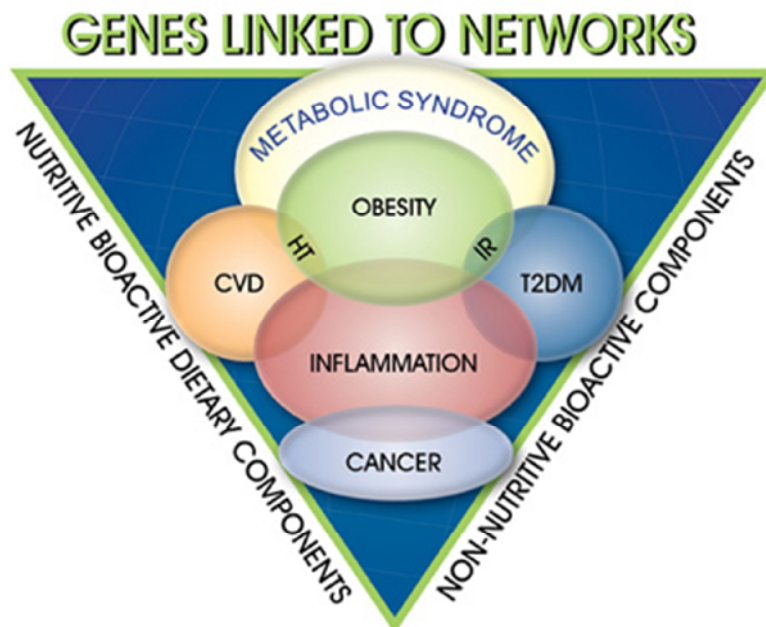


Figure 4

Genes linked to networks

Source :Mutch *et al* (2005)

Genetic approaches commonly used to identify the genes related to obesity include candidate gene and genome-wide association studies. Candidate gene studies find an association between variants in an individual's genome within or very near candidate genes and a disease of interest such as

obesity. Genetic studies have repeatedly demonstrated that some genes are associated at a higher frequency among the obese than in the non-obese individuals suggesting that a considerable proportion of weight variation may be due to genetic factors.

Knowing the genes related to obesity have far reaching effects individually and globally. Genetic information can be used to predict an individual's predisposition to the development of obesity and its complications. It also allows for the discovery of novel and personalized treatment strategies to be applied to different population groups being cognizant of the fact that inter-ethnic differences exist. The genetic and genomic studies being done among Asian populations will contribute greatly to the wealth of information on genetic predisposition to obesity. These unique and innovative genomic approaches and discoveries may lead to a better understanding of molecular pathways that give rise to obesity and can pave the way to better management and control of obesity, not only in Asia but throughout the world.

If the escalating population prevalence of obesity and its serious implications for public health are generally accepted with some notable exceptions, its causes and physiological consequences at the individual level are still elusive. In only a few decades, the industrialized world has gone from a calorie-poor to a calorie-rich environment. Obviously, the recent unlimited availability of low-cost calorie-dense food, along with increasing sedentarity, has played a major role in the adult obesity pandemic.

In the 1960s, Neel (1962) proposed the 'thrifty gene' hypothesis, whereby genes that predispose to obesity would have had a selective advantage in populations that frequently experienced starvation. People who possess these genes in today's obesogenic environment might be those that 'overreact' not just becoming slightly overweight, but extremely obese.

Obesity is an important disease with the potential for improved prevention using nutrigenetic knowledge. Arkadianos *et al* (2007) developed a personalised calorie-controlled diet, using 24 variants in 19 genes that were involved in

metabolism to a weight reduction programme. Further, compared weight loss and weight loss maintenance in 50 individuals who received exercise and dietary advice tailored to their genotype to optimise nutrient intake during weight loss and 43 control individuals who were given only generic diet and exercise advice. They were able to show that the group receiving personalised dietary advice not only performed better during the weight loss period, but also in weight loss retention over the following year.

The failure of current dietary guidelines in combating the obesity epidemic provides further evidence that the optimal dietary fat composition (amount and type of fatty acid) for optimal metabolic health is still unknown and that the traditional one size fits all approach does not work in the context of obesity and metabolic health. Pathogenesis of obesity is multifactorial and involves both genetics and environmental factors (Kelishadi, 2007)

Many genes are involved in regulatory pathways for weight gain and obesity. These genes include leptin, leptin receptors, melanocortin receptor 4, mitochondrial uncoupling proteins, peroxisome proliferator-activated receptor-gamma (PPAR γ), neuropeptide Y, and ghrelin as well as genes in signaling pathways(Mansoori *et al.*, 2015)

Peroxisome proliferator-activated receptor (PPAR)- γ is a transcription factor with a key role in adipocyte differentiation. Luan *et al* (2001) reported a gene-diet interaction with regard to PPAR γ Pro12Ala polymorphism. They showed an inverse association between polyunsaturated to saturated fatty acids ratio with BMI and plasma insulin levels in Ala carriers and in subsequent studies, the relationship between this polymorphism and nutrient intakes on BMI or waist circumference was verified (Vaccaro *et al.*, 2007). Thus, it might be possible that different dietary patterns between ethnic groups could modulate the relationship between BMI and this particular SNP.

The Peroxisome Proliferator Activated Receptor (PPAR) is given in figure 5

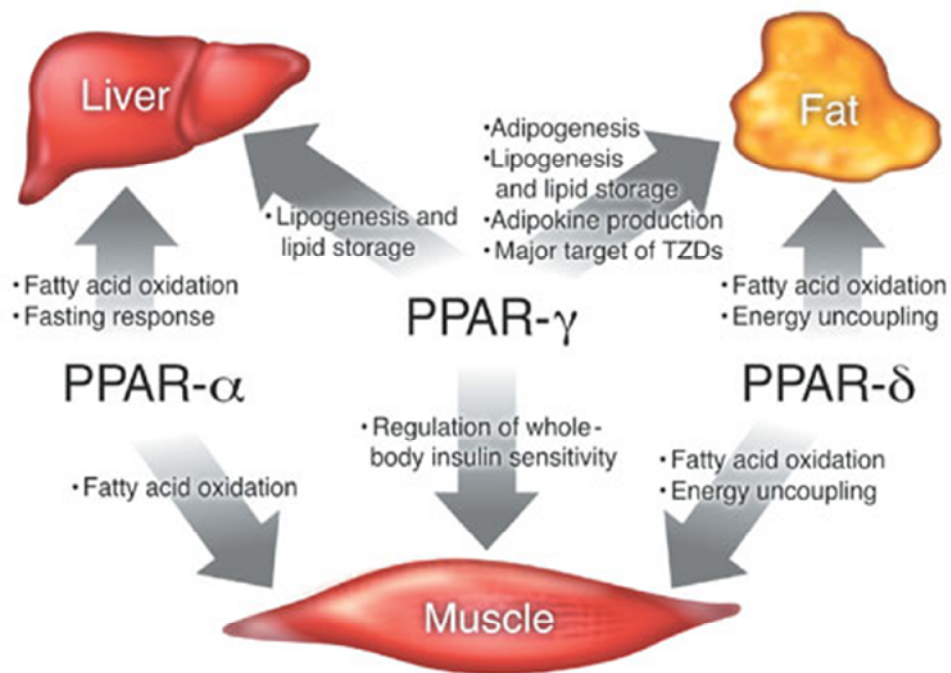


Figure 5

Peroxisome Proliferator Activated Receptor (PPAR)

(Source : Ronald *et al*, 2004)e

The peroxisome proliferator activated receptor (PPAR) is a member of the nuclear hormone receptor family, and consists of three subtypes: PPAR-alpha, PPAR-beta, and PPAR-gamma. In humans, alternative use of promoters and different splicing of PPAR-gamma results in three different isoforms: PPAR gamma 1, PPAR-gamma 2, and PPAR-gamma 3. The PPAR gamma 2 that is primarily expressed in white and brown adipose tissue can induce the differentiation of preadipocytes into adipocytes, regulate lipid and fatty acid metabolism, and enhance insulin sensitivity. PPAR- γ gene for sequence variants has identified two common polymorphisms. These are, respectively, a C→G substitution in exon B resulting in the conversion of proline to alanine at residue 12 of the PPAR- γ protein, and a synonymous C→T substitution at nucleotide position 161 in exon 6.(Globerman *et al.*, 2000)

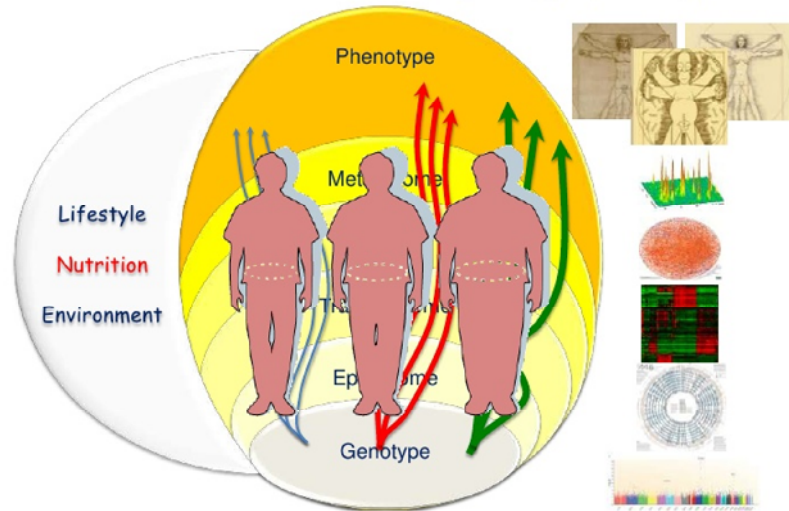


Figure 6

Nutrigenomics – Quantification of the nutritional genotype - Phenotype
 (Source : <https://www.pinterest.com/pin/638385315900004004>)

The recognition that nutrients have the ability to interact and modulate molecular mechanisms underlying an organism's physiological functions has prompted a revolution in the field of nutrition. Performing population-scaled epidemiological studies in the absence of genetic knowledge may result in erroneous scientific conclusions and misinformed nutritional recommendations. To circumvent such issues and more comprehensively probe the relationship between genes and diet, the field of nutrition has begun to capitalize on both the technologies and supporting analytical software brought forth in the post-genomic era. The creation of nutrigenomics and nutrigenetics, two fields with distinct approaches to elucidate the interaction between diet and genes but with a common ultimate goal to optimize health through the personalization of diet, provide powerful approaches to unravel the complex relationship between nutritional molecules, genetic polymorphisms, and the biological system as a whole. A genetic predisposition to obesity and possible impaired metabolic and appetite regulation make it difficult to lose and, more importantly, to maintain weight loss. Because of the psychological and physiologic impact of dieting, individuals should be encouraged to attain and maintain a reasonable body weight. Emphasise should be on increasing physical activity, a nutritionally

adequate intake, and moderate caloric restriction (250-500 Kcal less than the average daily intake as calculated from nutritional assessment) rather than weight loss.