FREE UNIVERSITY OF BRUSSELS
FACULTY OF MEDICINE
DEPT. OF GENERAL SURGERY

SURGICAL APPROACH TO OBESITY:

A REVIEW OF THE STATE OF THE ART

KATSANOS GEORGIOS MD, PhD

Supervisor: Dr. CEUTERICK MICHEL

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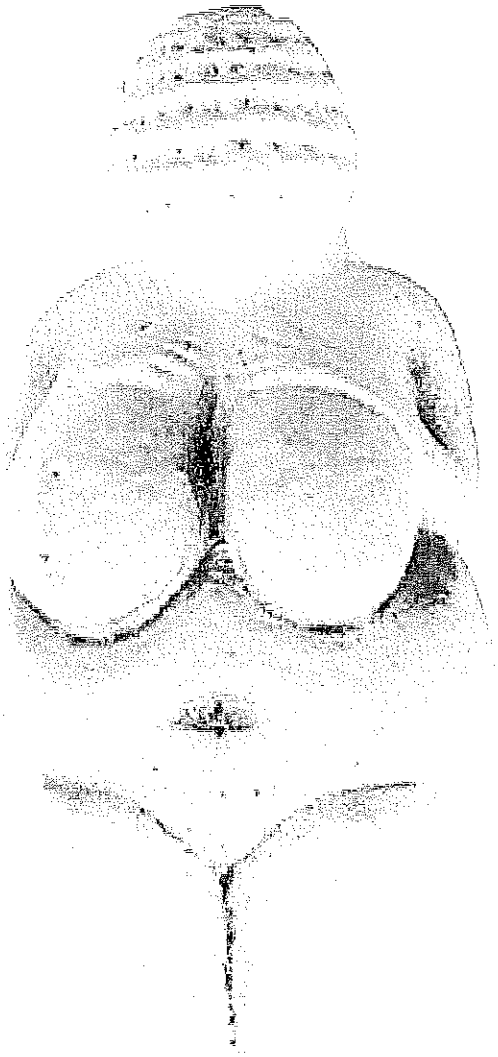


Venus of Willendorf
c. 24,000-22,000 BCE
Otolitic limestone
Naturhistorisches Museum, Vienna

"dis-moi, muse, cet homme subtil qui erra si longtemps, après qu'il eut renversé la citadelle sacrée de Troie. Et il vit les cités de peuples nombreux, et il connut leur esprit ; et dans son cœur, il endura beaucoup de maux, sur la mer, pour sa propre vie et le retour de ses compagnons."

HOMÈRE, Odyssée

Six years away from home is a long time....

Writing these lines I realize that a chapter of my life is coming to an end, as I am enjoying my last months in Belgium.

During these years, I met a lot of fabulous people that I would like to thank form the bottom of my heart for their help, their wisdom and their friendship, which is a valuable gift that I will treasure.

I would like to thank all my teachers for sharing their knowledge and transmitting their experience, and all my colleagues for the great moments we have shared during our training.

But above all, I would like to thank a person that amazed me with his personality and is an inspiration to everyone that has had the chance to work with him. A teacher, a mentor and I dare to say, a friend.

This work is respectfully dedicated to Dr. André Capron.

G. Katsanos

1rst Part: PRINCIPLES OF OBESITY

"Persons who are naturally very fat

are apt to die earlier than those who are slender."

Hippocrates, *Aphorisms. II-44*

1. DEFINITION OF OBESITY

Obesity is defined as an increased adipose tissue mass, or as the excessive accumulation of body fat[1], resulting in adverse health consequences:

"abnormal or excessive fat accumulation in adipose tissue, to the extent that health is impaired" (World Health Organisation, 2000).

The most widely used parameter for measuring obesity is the body mass index (BMI) which is defined as the weight/height^2 and measured in kg/m^2.

Given this definition, the status of obesity is attained when the BMI of a person exceeds 30, and the range from 25 – 29.9 is considered a state of "overweight".

Table 1 shows the classification of Obesity and BMI related health risks.

Table 1: Classification of obesity and BMI-related health risks (WHO)[2]

BMI (kg/m^2)	**Obesity Category**	**Health Risk w/o Medical Problems**	**Health Risk With Medical Problems**
< 19	Underweight	Slight	Minimal
19-24	Normal	None	Minimal
25-29	Overweight	Minimal	Moderate
30-34	Obese (WHO-I)	Moderate	High
35-39	Severe (WHO-II)	High	Very High
40-50	Morbid (WHO-III)	Very High	Extreme
50+	Super Obese	Extreme	Very Extreme

Fat distribution also has an important impact on health risk. Upper body obesity (abdominal obesity) is more strongly associated with a higher risk of the obesity related comorbidities. Fat distribution can be assessed by the ratio of waist-to hip circumference (waist/hip ratio) and visceral fat by waist circumference.

A waist circumference greater than 102 cm in males and 88 cm in females signifies medically significant obesity.

However, the above definitions are somewhat deceptive, as their wise simplicity should not undermine the complex behavioral, metabolic, genetic, environmental and hormonal mechanisms that contribute to the pathogenesis of a complex multifactorial chronic disease which tends to be the plague of the 21st century[2].

2. ENERGY BALANCE AND THE ADIPOCYTE

The major principle of energy homeostasis holds that when the energy input in the form of nutritients in a person equals the energy expenditure of that person, the body weight remains stable. When energy intake exceeds energy output, the excess energy is stored in the body mainly as fat and the overall body weight increases.

This energy balance in the human organism is regulated by a complex neuroendocrine feedback mechanism involving numerous pathways, with the hypothalamus playing the principal role in food uptake regulation. The detailed analysis of these mechanisms is beyond the scope of this chapter which will hopefully provide a brief outline of the physiological regulation of energy balance.

The first breakthrough in the understanding of food intake regulation came from the observation that patients with Frölich's syndrome with lesions in the basal hypothalamus presented severe obesity. Experimental animal models with basal hypothalamic lesions were produced and the theory of the central role of the hypothalamus in food intake regulation became clearer[3].

Today, more than 60 years later we have witnessed a great advance in the understanding of these complex mechanisms of energy homeostasis, yet the fine details are still to be discovered.

Four major categories of stimuli influence the hypothalamic mechanisms:

1. metabolites (such as glucose)
2. neural afferents (vagus nerve stimulated by gut distention)
3. hormones such as leptin, insulin, cortisol glucagon like peptide 1 (GLP-1), gastric insulin related peptide(GIP), oxyntomodulin, apolipoprotein 4 (ApoA-4), amylin, and PYY3-36

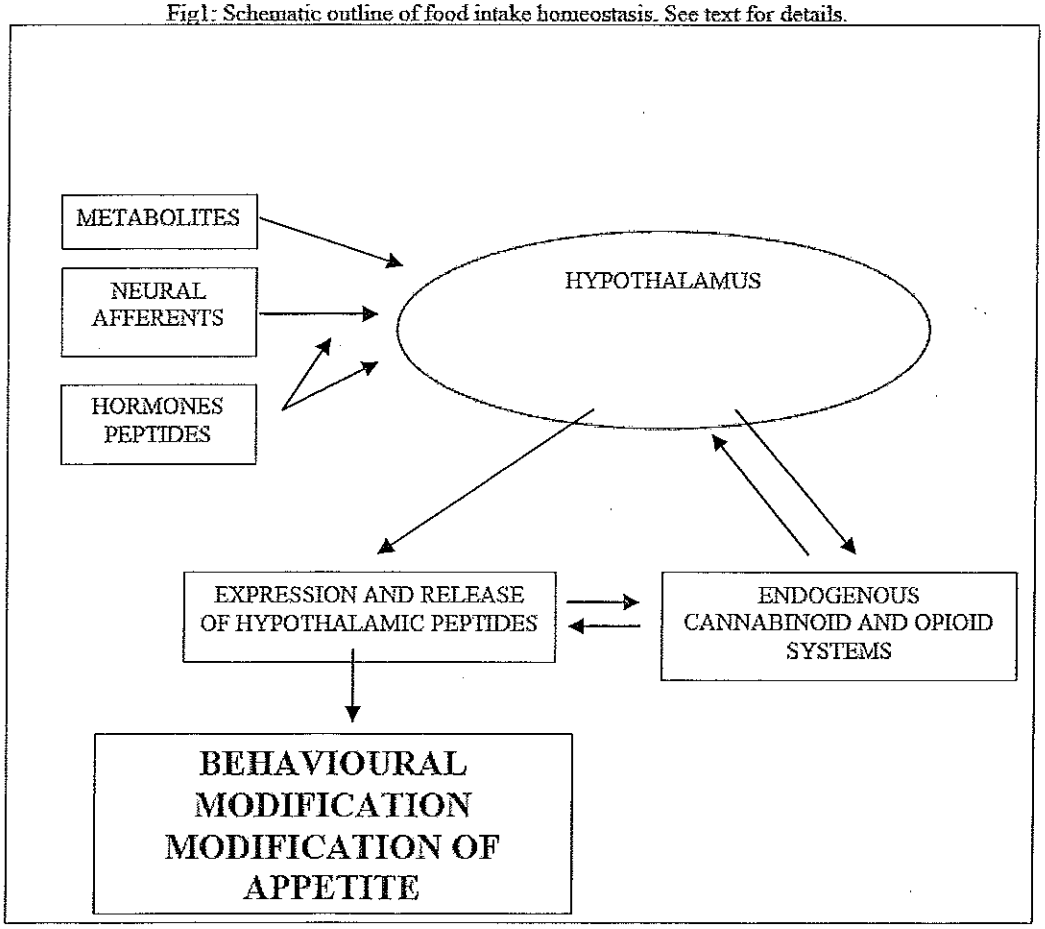
4. peptides such as ghrelin (the only orexigenic peripheral circulating peptide), peptide YY, cholecystokinin

These signaling pathways influence the expression and release of hypothalamic peptides such as neuropeptide Y (NPY), agouti related peptide (AgRP), melanocyte stimulating hormone (a-MSH) and melanin concentrating hormone (MCH).

This hypothalamic response aiming at energy homeostasis involves a variety of systems and processes, including endocrine adjustments, behavioural changes, the endogenous cannabinoid and opioid systems[4] as well as sympathetic and parasympathetic nervous system outflow modifications, resulting in food intake modification[5,6,7].An outline of these mechanisms is depicted in fig1:

Fig1: Schematic outline of food intake homeostasis. See text for details.

Fig1: Schematic outline of food intake homeostasis. See text for details.



Traditionally, the adipocyte was considered a simple storage cell that stores up excess energy in the form of triacylglycerol (triglycerides) and releases free fatty acids and glycerol in periods of fasting. But today the adipocyte is recognized as an elaborate endocrine and paracrine cell[8] that secrets factors such as leptin, adiponectin, TNF-α, IL-6, resistin and angiotensinogen, influencing directly energy homeostasis and lipid metabolism[9,10] , immune response[11], vascular homeostasis[12], steroid hormone activation[13], etc. So the recent advances in understanding the function of adipocytes and the pluripontent influence of adipocytokines[14] revealed the strikingly immense capability of these cells to affect homeostasis on more than one way…

In times of plenty, the size and total number of adipocytes increases. The total mass of adipocytes plays an important role in the pathogenesis and the morbidity of obesity.

3. PATHOGENESIS OF OBESITY

A simplistic approach to the pathogenesis of obesity would be to simply state that it occurs when energy intake exceeds energy expenditure for long periods, resulting in increases adipogenesis and increases overall body fat cell deposition. But the mechanisms responsible for this imbalance in energy homeostasis are multifactorial and complex, combining the interaction between genetics, behaviour and the environment.

3.1. Increased energy uptake (dietary obesity)

The downside of living in times of plenty in the industrialized countries has resulted in a great abundance of food, high in energy value, easy to find and accessible to all, adults and children. On the other hand, ingestive behavior is governed by intricate cognitive and developmental factors deeply impringed in the human DNA[15]. In the concluding remarks to "The Origin of Species" Charles Darwin noted that "The evolution of higher animals directly follows. . . from the war of nature, from **famine** and death. ..[16]" We are all programmed to eat.

3.2 Decreased energy expenditure

Industrialisation provided machines to do the work for us, cars to transport us and closed urban environments favouring "mental" work and decreasing physical activity demands, in such a degree that a typical European or American urban citizen has to actively seek physical activity in the forms of gyms, sports, etc.

With the physical activity diminished, the alternative pathways for "burning" energy are the basal metabolic rate and the dietary thermogenesis which is the energy expenditure that follows the ingestion of a meal. Ingestion is a rather inefficient process, as heat produced by eating may dissipate up to10% of the ingested calories.

In the obese, the thermic effects of food are reduced particularly in individuals with impaired glucose tolerance or diabetes. So the most efficient target for weight reduction is the augmentation of the physical activity, which is more easily said than done[17].

It is now recognised that cultural and social interactions with environmental factors play a key role in the pathogenesis of obesity. In table 2 there is a list of the factors contributing in the pathogenesis of obesity[2]:

Table2: Factors influencing the pathogenesis of obesity

Social factors	**Cognitive factors**
• changing social structures	• dietary restraint
• economic restructuring and transition to market economies	• attitude about body weight
• urbanization	
• socio-economic status	
Cultural factors	**Biological factors**
• cuisine and food selection	• fat content of diet
• attitude toward health	• energy intake
• body image	• reduced physical activity

3.3 Leptin deficiency and Leptin resistance

Leptin plays a key role on the metabolic regulation pathways[1], having the property to evoke satiety signals at the hypothalamus. A stated below, laboratory animals with leptin deficiency present with increased appetite and obesity. Leptin deficiency has been described in humans however the majority of obese patients paradoxically have increased serum leptin concentration. The explanation for this is that either the increase of adipocyte mass provokes a leptin resistance with down-regulation of the hypothalamic receptors for leptin[18], or that there is a deficiency in brain transport of leptin, or both[19].

3.4 Drug induced weight gain

Treatment of diabetics with insulin, sulfonylureas or thiazolidinediones, but not metformin can increase hunger and food intake, resulting in weight gain. Treatment with some antidepressants, antiepileptics and neuroleptics can also increase body weight, as can cyproheptadine, probably through effects on the monoamines in the central nervous system[20].

3.5 Syndromic Obesity

Syndromic obesity is obesity occurring in the clinical context of a distinct set of associated clinical phenotypes[21]. More than 25 entities of syndromic obesity have been described and recently the genetic base of these diseases have been thoroughly studied, shedding more light in the pathophysiology. However the exact mechanisms of these syndromes are not yet fully elucidated. It is believed that syndromic obesities and their elucidation might provide models for medical targeting of obesity pathways. In table 3, a brief description of the most representative forms of syndromic obesity is presented:

Table3: Reproduced and modified from ref. 14

Syndrome	Gene	Chromosomal location	Mode of inheritance	Phenotype
PWS Prader–Willi syndrome	Contiguous gene disorder	15q11–13	Imprinting defect with loss of paternally expressed genes on 15q11–13	Neonatal hypotonia; poor feeding; evolving into extreme hyperphagia; central obesity; decreased lean body mass; short stature; hypothalamic hypogonadism; mild mental retardation and obsessive compulsive behavior.
BBS Bardet–Biedl syndrome	At least eight loci (BBS1–BBS8) Seven genes identified	BBS1: 11q13 BBS2: 16q21 BBS3: 3p12–13 BBS4: 15q22–23 BBS5: 2q31 BBS6 (MKK5): 20p12 BBS7: 4q27 BBS7: 4q27 BBS8 (TTC8): 14q32	Oligogenic: either autosomal recessive or tri-tetra allelic	Progressive rod-cone dystrophy; post axial polydactyly; renal cysts; progressive renal disease; dyslexia; learning disabilities; hypogonadism; occasional congenital heart disease and progressive late childhood obesity.
Alström Syndrome	ALMS1	2p13	Autosomal recessive	Mild truncal obesity; short stature; type 2 diabetes; retinopathy; sensorineural hearing loss; nephropathy and dilated cardiomyopathy.
Cohen syndrome	VPS13B	8q22–23	Autosomal recessive	Mild truncal obesity; thin extremities; short stature; mild mental retardation; microcephaly; dysmorphic features; hypotonia; joint laxity; intermittent neutropenia and retinochoroidal dystrophy.
Borjeson–Forssman–Lehmann Syndrome	PHF6	Xq26	X-linked dominant	Late childhood truncal obesity; short stature; gynecomastia; hypotonia; poor feeding; large ears; small genitalia; mental retardation; microcephaly and epilepsy.

3.6 Non-syndromic monogenic obesity

Single gene alterations that cause obesity have been described in rodents and later in humans[22], and helped to better understand the metabolic pathways implicated. Although rare, these forms of obesity exist in the form of leptin or leptin receptor and melanocortin 4 receptor gene deficiency[21]; early data show that recombinant leptin subcutaneous administration can have beneficial effect in patients with genetically derived leptin deficiency[23].

3.7 Neuroendocrine obesity

Craniopharyngioma, basal scull tumors and diseases that affect the hypothalamic function affecting energy homeostasis can be rare causes of severe obesity.

Cushing syndrome, hypothyroidism and insulinomas are other endocrine causes of secondary obesity and treatment should be primarily directed to the underlying hormonal abnormality.

All these aforementioned mechanisms have a common end result: The dysregulation of energy homeostasis and the promotion of adipogenesis, resulting in obesity.

3.8 Eating disorders

Binge eating disorder, night eating syndrome, bulimia nervosa etc are syndromes predisposing to uncontrolled energy uptake.

4. PATHOPHYSIOLOGY OF OBESITY

The phenotypic impact of obesity is not welcome in modern societies which promote thin athletic models of life, and obese persons are confronted daily with body image issues[24] and discriminatory behavior[25], experiencing important impacts in social and professional activities affecting their overall quality of life[26].

Unfortunately, the phenotypic social issues of obesity is only the tip of the iceberg, because obesity has an important impact on general health and in fact is a multifactorial multisystemic chronic disease.

4.1 Obesity and associated comorbidities:

An obese person is exposed to various comorbidities such as Cardiovascular disease, Hypertension, Dyslipidemias, Diabetes type II, Sleep apnea and Degenerative joint disease.

4.1.1 Obesity and the Heart:

Obese persons have higher cardiac output and lower peripheral resistance than lean individuals, due to the increased metabolic demand induced by excess body weight. This results in elevated left ventricular filling pressures, increased ventricular wall stress and ventricular eccentric hypertrophy[27]. Increased filling pressures are also responsible for the increased risk that obese individuals have for developing atrial fibrillation, as a result of atrial overfilling and dilatation[28].

But the increased adipose tissue mass causes also local mechanical cardiac problems, either by the increased pericardial adiposity which can interfere directly with cardiac and pericardial function, or by fatty infiltration of the myocardium, a result of local metaplastic changes, which alters the quality of myocardial contractility (Adipositas Cordis)[29] In table 4, the electrocardiographic changes frequently observed in obesity are shown[30]. The end result of increased adiposity is

predisposition to congestive heart failure[31] and/or to conduction abnormalities and cardiac arrhythmias[32].

Tabe 4: ECG changes that may occur in obese individuals

ECG Changes
↑ Heart rate
↑ PR interval
↑ QRS interval
↓ QRS voltage
↑ QTc interval
↑ QT dispersion
ST-abnormalities
ST depression
Left-axis deviation
Flattening of the wave (inferolateral leads)
Left atrial abnormalities
False-positive criteria for inferior myocardial infarction

4.1.2 Obesity and the Vessels

The endocrine and paracrine elaborate functions of the adipocyte combined with the total adipocyte number and size increase in obesity, result in an endocrine humoral imbalance exposing the organism to a "proinflammatory state" with an increased release of cytokines, CRP and vasoactive substances. This has a direct impact on the vascular system, with an augmentation of endothelial oxidative stress[33], endothelial dysfunction[34] and damage, vasoconstriction and predisposition towards hypertension[35], coronary artery disease[36], atheromatosis[37], stroke[38] and venous disorders like deep venous thrombosis[39] and pulmonary embolism[40].

4.1.3 Obesity and Diabetes

Expansion of adipose tissue mass has been shown to decrease insulin responsiveness and result in glucose intolerance and type II diabetes. Decreased insulin responsiveness is mainly mediated by two mechanisms: Insulin receptor down regulation, and spatial modification of the receptor mediated intracellular glucose transport system that diminish its effectiveness, due to cell membrane expansion[41].

The decrease in number and responsiveness of the insulin receptors are directly associated with obesity. In a state of chronic positive energy balance, fatty acids that are synthesised and stored, directly downregulate the number of insulin receptors in cells[42]. This results in decreased muscle, liver and adipose tissue responsiveness to insulin, hyperglycaemia and diabetes, with all the devastating multisystemic complications.

4.1.4 Obesity and the Lung

The body fat accumulation around the thoracic wall creates a restrictive ventilatory component in otherwise healthy obese subjects[43]. The severity of those restrictive phenomena is directly associated with the BMI, and are reported up to 56% decrease in total lung capacity in morbid obese persons[44]. Restriction is furthermore aggravated by abnormal diaphragmatic position and mobility, secondary kyphosis and muscle mass decrease or muscle atrophy.

The end result is a substantial decrease in functional residual capacity and suboptimal efficiency of lung mechanics.

Obesity is a classic example of ventilation perfusion mismatch with alveolar hypoventilation that was referred to as "the Pickwick syndrome"

A major issue of respiratory function in the obese is the sleep apnea, as obesity is considered the major modifiable risk factor in sleep disordered breathing[45]. Sleep apnea is considered a risk factor for pulmonary and systemic hypertension, congestive heart failure, myocardial infarction, dysrhythmias and stroke, as well as increased mortality rates[46].

4.1.5 Obesity and the Kidney

Obesity is "nephrotoxic" in otherwise health subjects[47] and obese persons are exposed to an increased risk of kidney disease. The mechanisms underlying the nephrotoxic effects of obesity are mediated by endothelial dysfunction, vasoconstriction, oxidative stress, microalbuminuria, glomerular injury and focal segmental gromerulonephritis, all observed in obese patients. In addition to these inherent noxious effects, when obesity is complicated with hypertension and diabetes, the detrimental impact on kidney function is multiplied[48]. Treatment of obesity should be a priority in patients with chronic glomerular disease[49].

4.1.6 Obesity and The Metabolic Syndrome

"Whichever definition is used and whatever the variation in the numbers due to the different criteria, when looking at prevalence data for the metabolic syndrome in different countries and across various ethnic groups, one fact is clear. Universally, the metabolic syndrome is a huge problem and is one that is growing at an alarming rate".

Professor Sir George Alberti, International Diabetes Federation, 2003

The lethal and insidious clustering of cardiovascular risk factors in an individual is currently recognized as the metabolic syndrome or syndrome X.

The metabolic syndrome is defined as the simultaneous occurrence of the following cardiovascular risk factors:

- Abdominal obesity
- Atherogenic dyslipidemia
- Raised blood pressure
- Insulin resistance and/or glucose intolerance
- Proinflammatory state
- Prothrombotic state

According to the new IDF definition, for a person to be defined as having the metabolic syndrome they must have:

- Central obesity (defined as waist circumference $\geq$ 94cm for Europid men and $\geq$ 80cm for Europid women, with ethnicity specific values for other groups) plus any two of the following four factors:

- raised TG level: ≥ 150 mg/dL (1.7 mmol/L), or specific treatment for this lipid abnormality
- reduced HDL cholesterol: < 40 mg/dL (1.03 mmol/L) in males and < 50 mg/dL (1.29 mmol/L) in females, or specific treatment for this lipid abnormality
- raised blood pressure: systolic BP ≥ 130 or diastolic BP ≥ 85 mm Hg, or treatment of previously diagnosed hypertension
- raised fasting plasma glucose (FPG) ≥ 100 mg/dL (5.6 mmol/L), or previously diagnosed type 2 diabetes. If above 5.6 mmol/L or 100 mg/dL, oral glucose tolerance test is strongly recommended but is not necessary to define presence of the syndrome.

Obesity is currently considered as the main etiology of the rising on the prevalence of the metabolic syndrome, which has a common end point: Cardiovascular disease and increased morbidity and mortality.

The pathophysiology of the metabolic syndrome is underlined by three major etiologic categories: Obesity, Insulin resistance and a cluster of independent factors like dyslipidemias and hypertension[50]. The proinflammatory and prothrombotic state are results of the adipocyte derived adipocytokines, an example of the potent capacity of a once considered "simple" cell to modify the humoral environment and to provoke generalized alteration in inflammatory response and in coagulation homeostasis[51].

Patients with the metabolic syndrome are twice as likely to die from and three times as likely to have a heart attack or stroke compared with people without the syndrome[52]. These alarming data underline the impact of obesity in general health status and its implications in population morbidity and mortality.

4.1.7 Other problems associated with Obesity

Melanoma, colon cancer, renal cell carcinoma, degenerative joint disease, dermatologic disease, gallbladder stones, reproductive disorders, idiopathic intracranial hypertension and psychosociological issues are just some of the complications of the obesity epidemic, contributing to the morbidity and mortality of this complex disease. A summary of obesity related medical complications is presented on Table 5:

Table 5: Medical complications of obesity.

Gastrointestinal	Gallstones, pancreatitis, abdominal hernia, NAFLD (steatosis, steatohepatitis, and cirrhosis), and possibly GERD
Endocrine/metabolic	Metabolic syndrome, insulin resistance, impaired glucose tolerance, type 2 diabetes mellitus, dyslipidemia, polycystic ovary syndrome
Cardiovascular	Hypertension, coronary heart disease, congestive heart failure, dysrhythmias, pulmonary hypertension, ischemic stroke, venous stasis, deep vein thrombosis, pulmonary embolus
Respiratory	Abnormal pulmonary function, obstructive sleep apnea, obesity hypoventilation syndrome
Musculoskeletal	Osteoarthritis, gout, low back pain
Gynecologic	Abnormal menses, infertility
Genitourinary	Urinary stress incontinence
Ophthalmologic	Cataracts
Neurologic	Idiopathic intracranial hypertension (pseudotumor cerebri)
Cancer	Esophagus, colon, gallbladder, prostate, breast, uterus, cervix, kidney, skin (melanoma)
Postoperative events	Atelectasis, pneumonia, deep vein thrombosis, pulmonary embolus abdominal compartment syndrome

5. Prevalence of obesity

In the Geneva 2000 report, the World Health Organisation characterised the problem of obesity as a global epidemic[53], raising the alarm on the international community, as more than a billion people are overweight worldwide and 300 million are obese, while projections for the future are estimating a significant increase in these numbers, unless adequate global measures are taken..

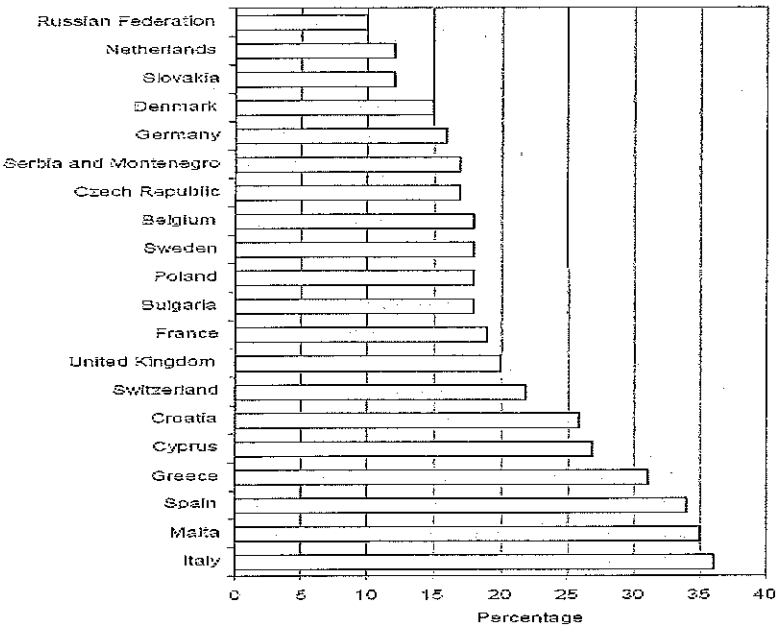
Since 1980, the prevalence of obesity has risen 3 fold in the European region, and at these rates, it is estimated that about 150 million adults will be obese by 2010. With these rates, in just five years in the European region the number of obese people will rise by 20 million. Furthermore, all countries, even the ones with traditionally low rates of overweight and obesity such as France and the Netherlands, show an upward trend in their numbers. Further, while the prevalence in the European Region is expected to rise by an average of 2.4% in women and 2.2% in men over five years, some countries might show a faster increase, such as Finland, Germany, Greece, Sweden and the United Kingdom for men and Georgia, the Republic of Moldova, Slovakia and Tajikistan for women[54].

Currently the prevalence of obesity in the European region is estimated at 26%, and unfortunately the prevalence of overweight ranges from 25 to 75%, having passed 50% of the population in many countries (including Belgium) and continuing to rise.

Numbers are also alarming in the United States, where obesity reaches 31% and following a steady upward trend[55].

Unfortunately, the future does not seem very bright, as obesity strikes also children at very high rates and is actually considered an acute health crisis in the paediatric and adolescent population[56]. 10–30% of European children aged 7–11 years and 8–25% of adolescents (14–17 years) are overweight or obese[57] (fig 2).

Fig 2 :Prevalence of overweight and obesity in children 7–11 years in the WHO European Region[59]



The latest reports of WHO concerning the prevalence of obesity (BMI>30) is presented in the following figures (fig 3 – 6)

Fig 3: Prevalence of Obesity, age 15 and above. Source: OECD factbook 2005

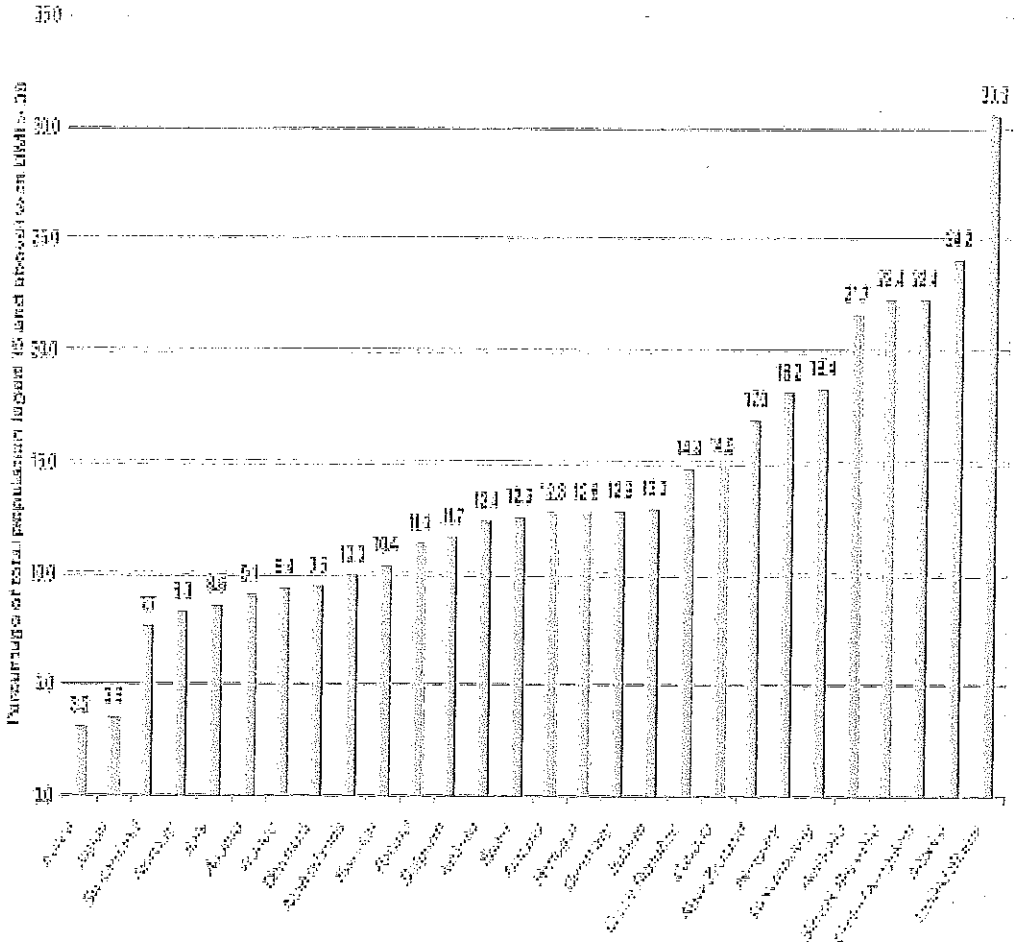


Fig 4: Projections of male obese persons from the age of 30 in Belgium

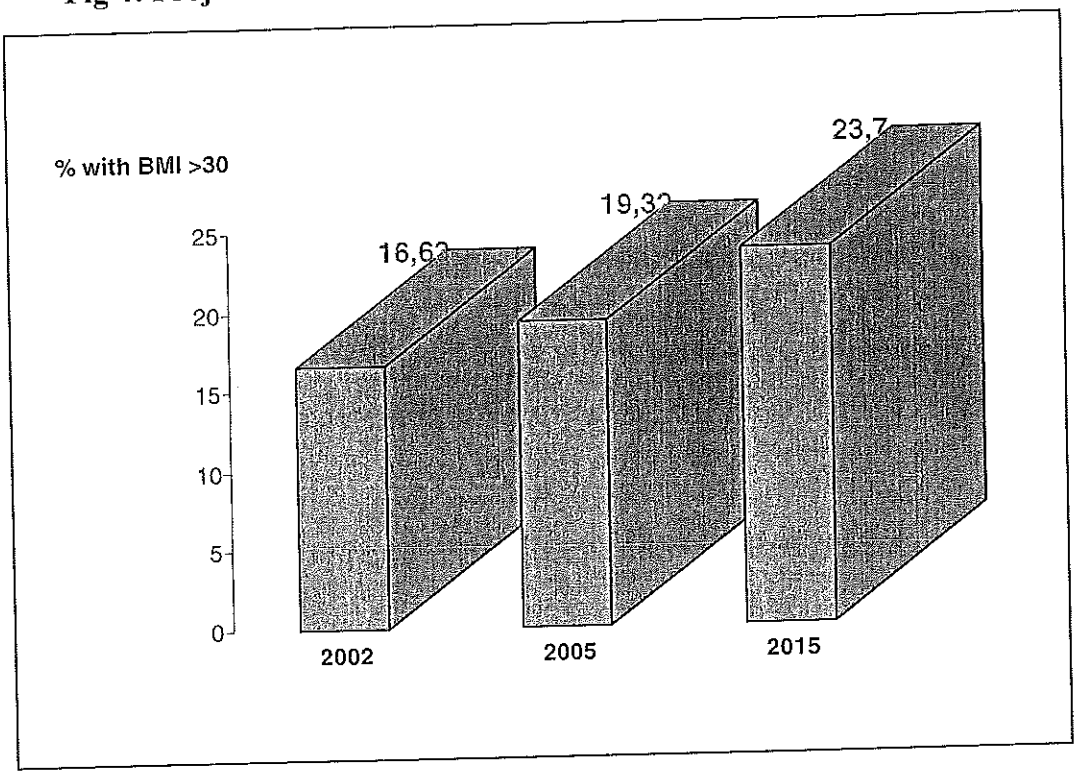


Fig 5: Projections of female obese persons from the age of 30 in Belgium

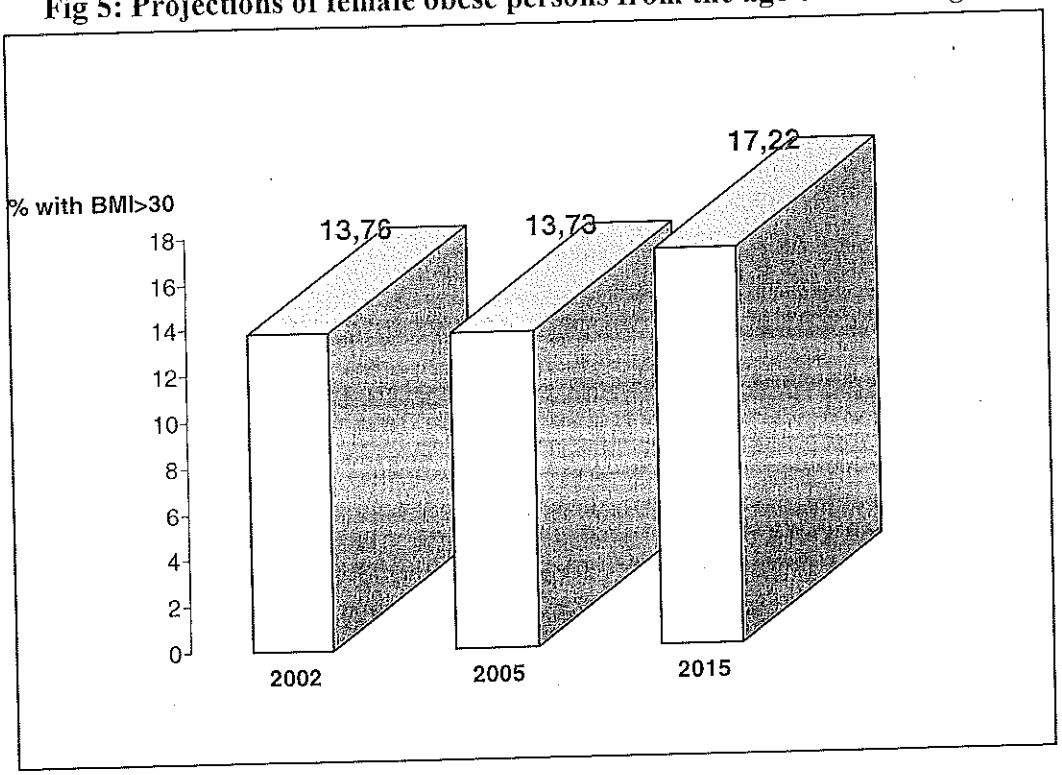
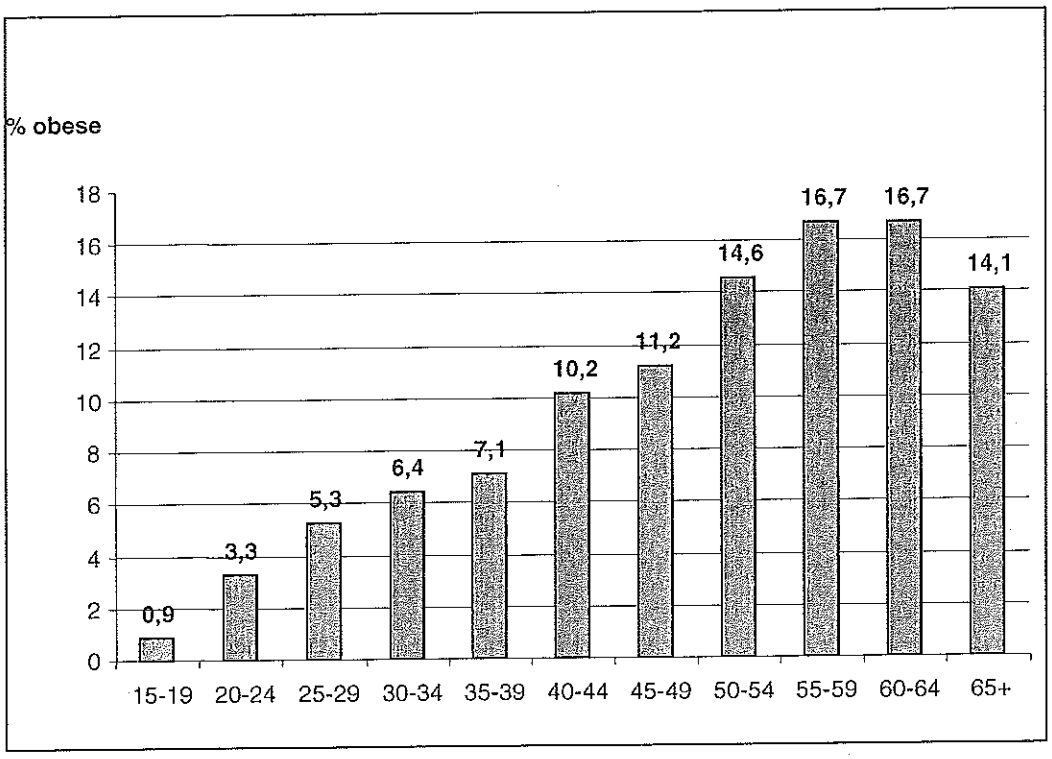


Fig 6: Obesity prevalence in Belgium in different age groups - Both sexes



Obesity is spreading in an alarming rate and the statistics of the world health organisation as illustrated in the following pages depict graphically the globalisation of the problem and the future projections of this pandemic (fig 7-10):

Fig 7: Prevalence of obesity in males, year 2005

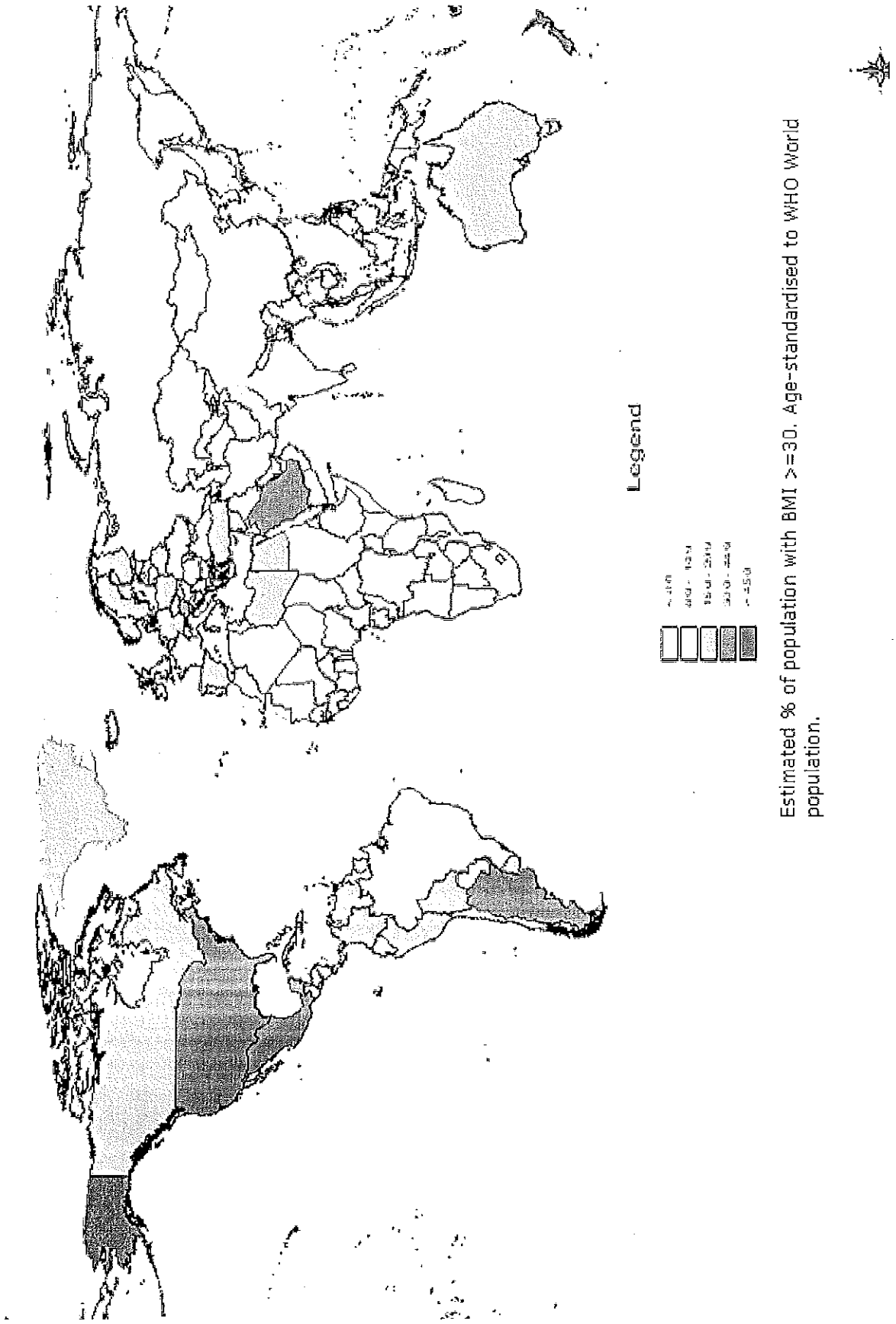


Fig 8: Prevalence of obesity in males, year 2015

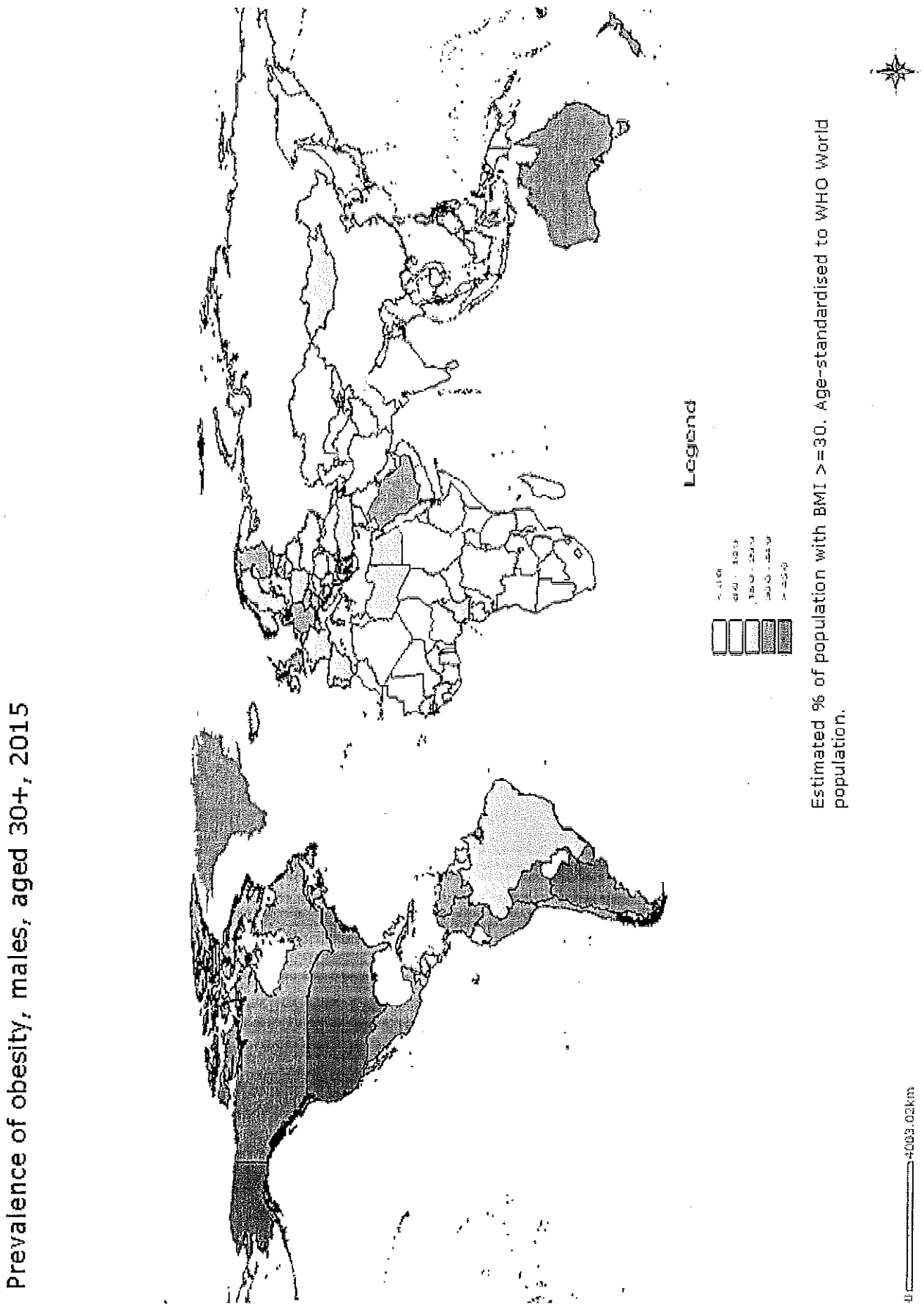


Fig 9: Prevalence of obesity in females, year 2005

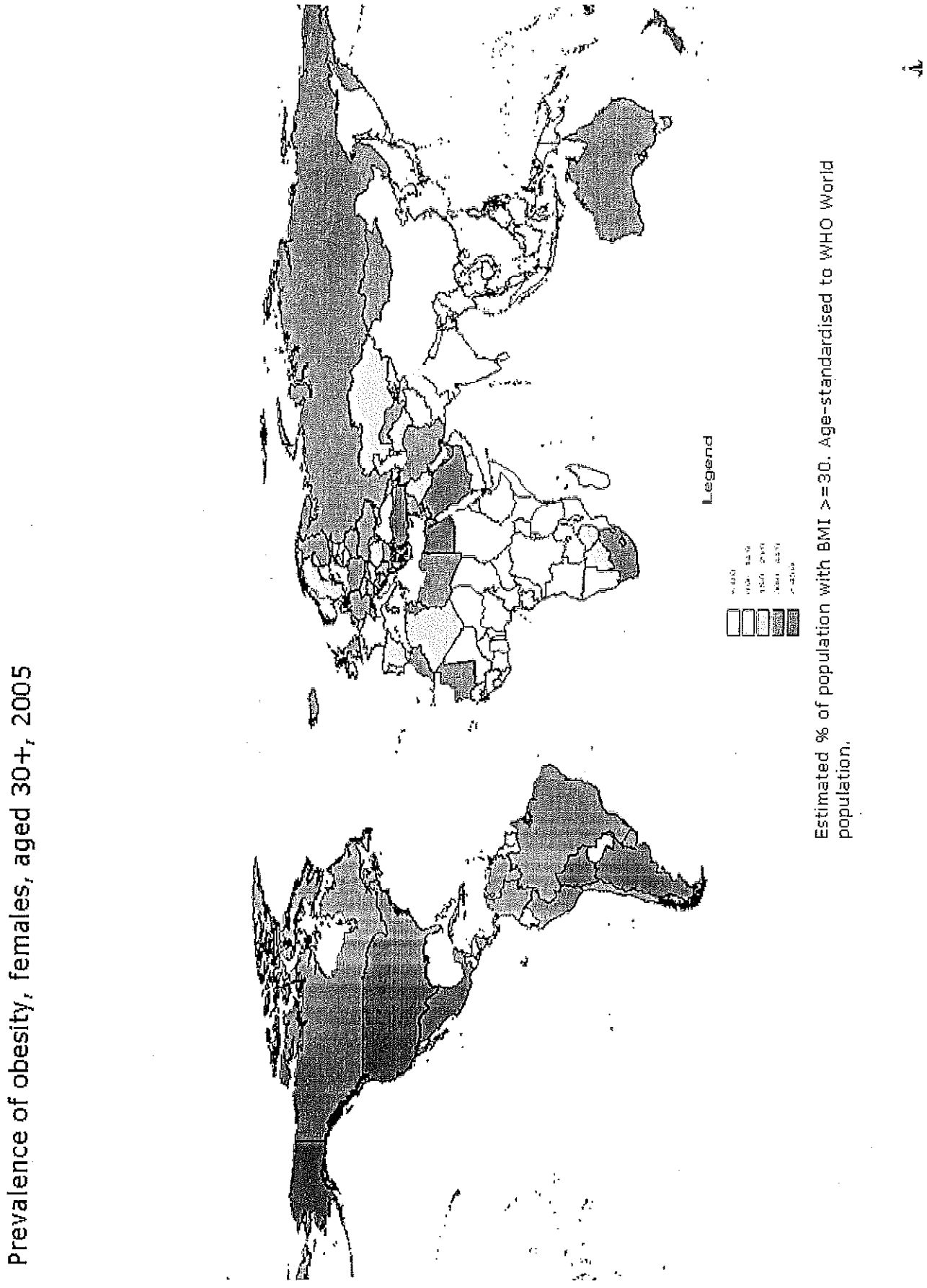
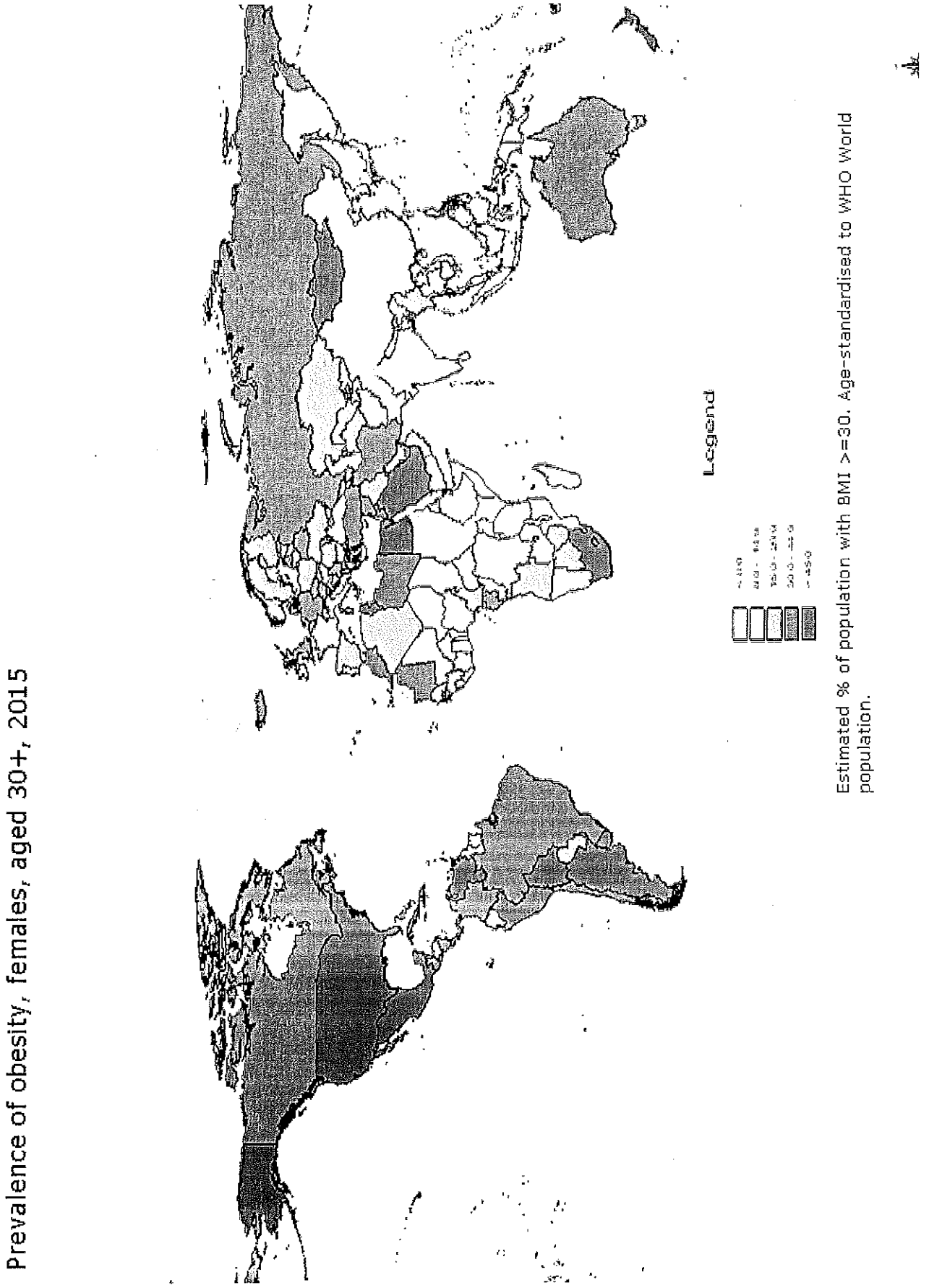


Fig 10: Prevalence of obesity in females, year 2015



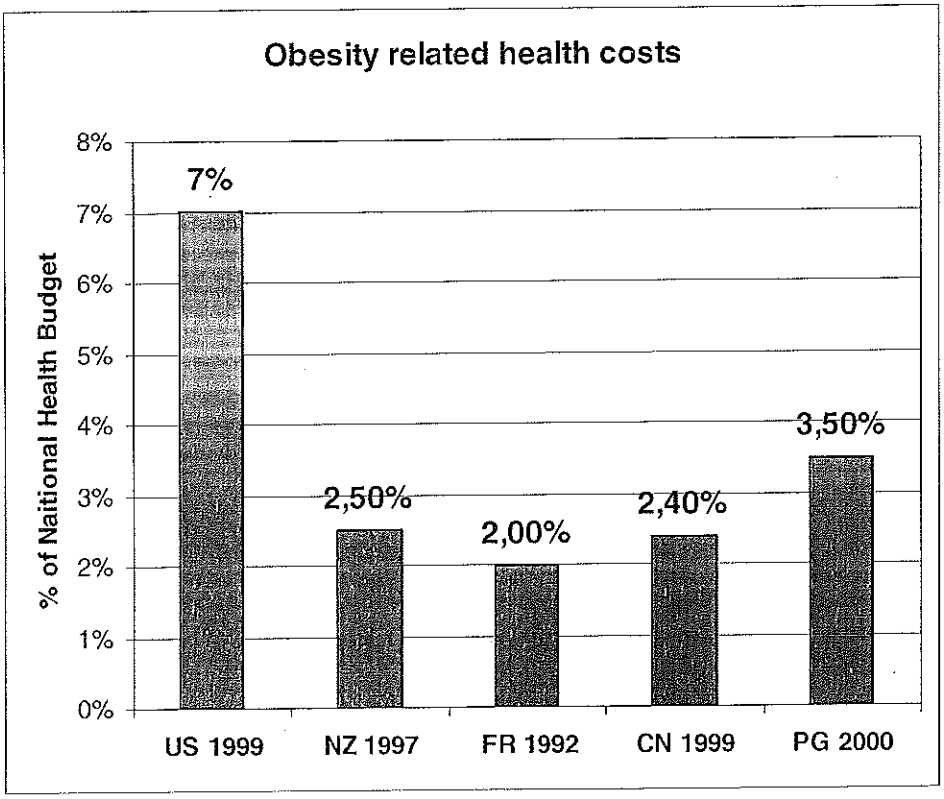
6. The Cost of Obesity

Obesity is a chronic debilitating disease with significant morbidity and its rapid spreading has posed new challenges to national health marketing and management throughout the countries affected.

Currently, an estimated 2 – 8 % of total national health budgets is used for treatment of obesity related diseases[58].

Through out the literature the estimated cost burden of obesity in national health budgets is estimated at 7.0% for the US[59] (1999), 2.5% in New Zealand[60] (1997), 2.0% in France[61] (1992), 2.4% in Canada[62] (1999) and 3.5% in Portugal[63] (2000). Although these studies are differently designed, in different period and even with different BMI cut-off points, they give a general idea of the heavy cost of obesity to the society. A schematic depiction of total health costs for obesity in different countries and in various periods is presented in fig 11.

Fig 11: % of national health budget spend on obesity



The conclusion of all the studies that were analysed was that the cost burden of obesity naturally follows its epidemiologic upward trend world wide, and an obese person will require a 36-37 % increase in annual health costs (data from C.D.C.).

It is estimated that, in 2002, the total cost of obesity in the EU was €32.8 billion. This estimation is based on extrapolation of the data from the UK National Audit Office Report, which calculated the direct and indirect health care costs associated with obesity in 1998, and the prevalence of obesity within the EU member states Actually, obesity health related cost is estimated to 5% of European countries national health budget (ranging from 2 to 8 %). (Data from the LipGene - EU Sixth Framework Programme Integrated Project 2004-2009).

This depicts the impact of obesity not only in the affected people's health, but in general public health, as it absorbs great amounts of funds and contributes considerably in the design and planning of national and international health budgets.

7. Obesity and Quality of Life

A considerable number of studies have addressed the issue of the impact of obesity in quality of life and they all agree on the heavy impact of this condition in everyday life. Obese persons experience a negative impact of obesity in their physical activity, self-esteem, psychosocial status they have poorer health, mood variations and manifest a poor social life activity[64]. Depression and low self esteem are common findings[65].

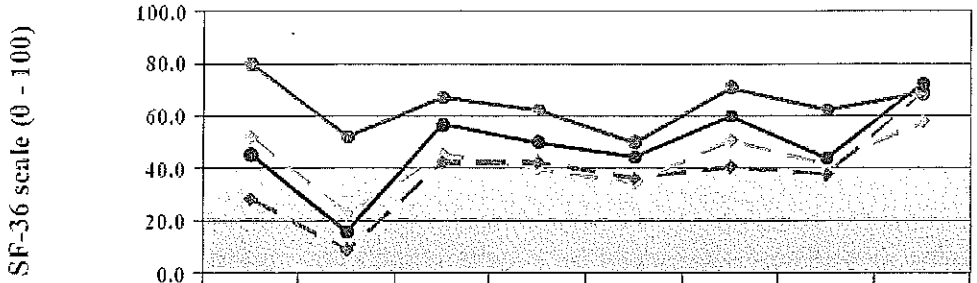
Obese persons have a worse social activity even when they are compared not only with healthy subjects, but also with patients suffering from other chronic diseases, like rheumatoid arthritis and peripheral arterial vascular disease and have poorer mental health than cancer survivors[66].

Interestingly, quality of life indexes almost uniformly rise when weight reduction occurs, either by medical or surgical means[67].

Another conclusion of the studies analysed was that the impact of obesity on quality of life is more intense in premenopausal women than in any other group, a reflection of modern society esthetic standards and models.

A recent UK study by Anette Wohl titled: "The existing and projected impact of obesity on the health service and society in the United Kingdom" (Faculty of Economics and Social Science, Christian-Albrechts-University of Kiel), the author stresses the unfavourable impact of increased BMI in quality of life. (fig 12)

Fig 12 : SF-36 QOL and BMI in the UK. From the dissertation thesis A. Wohl, with the authors permission.



	Physical Functio-ning	Role Physical	Bodily Pain	General Health	Vitality	Social Functio-ning	Role Emotio-nal	Mental Health
BMI = 40 kg/m²; age 18 - 54	51.9	22.7	45.5	39.6	34.4	50.6	41.3	57.7
BMI 18.5 - 24.9 kg/m²; age 18 - 54	79.7	52.1	67.0	62.2	49.8	70.7	62.1	68.5
BMI = 40 kg/m²; age ≥ 74	28.4	8.8	42.3	42.2	36.1	40.6	37.6	69.2
BMI 18.5 - 24.9 kg/m²; age ≥ 74	45.3	15.6	56.6	49.8	44.1	59.6	43.7	72.0

SF-36 health dimension

8. Medical Treatment of Obesity

The classic strategy for treatment of obesity is to inverse the positive energy balance and to create a nutritional state where energy input is lower than energy expenditure resulting in weight loss. The most conventional and widely used measure to achieve weight loss is thus diet and augmentation of physical activity. However, although diet and augmentation of physical activity can result in significant loss of weight, their long term effects are often limited as relapse and weight re-gain often occur[68].It is beyond the scope of this chapter to analyse the different diet strategies that can be employed in an adapted weight loss program, and we will provide a brief outline of the medical treatment of obesity today.

One elementary principle of current pharmacotherapy for obesity is that medicine will have their optimal effect only when combined with behavioural modification and diet. When pharmacotherapy is interrupted, weight regain and relapse occurs, just like with other chronic diseases: Interruption of medication leads to relapse[69].

Adults with BMI of ≥ 27 with obesity-related co morbidities or those with a BMI ≥ 30 with no co morbidities, may be considered eligible for pharmacotherapy[70].

There are two major categories of drugs for obesity, the peripheral acting drugs acting my malabsorption mechanisms, and the centrally acting anorexigenic drugs.

Orlistat: A non absorbed intestinal lipase inhibitor which blocks intestinal fat absorption by 30%. It is the only peripheral acting obesity drug, and with good compliance a loss about 10% of weight occurs, which is maintained as long as orlistat is continued. The major draw back in the use of this agent is the decreased patient

compliance due to gastrointestinal side effects, especially when ingested fat exceeds 70 gr.

Sibutramine is a serotonin noradrenalin re-uptake inhibitor. It has a double action, reducing food intake by enhancing satiety and increasing energy expenditure by increased thermogenesis. Its results are similar of those of orlistat

Serotonin agonists fenfluramine and dexfenfluramine have been removed from the market because of reports that they produce cardiac valve abnormalities.

Orlistat and sibutramine are the main prescribed medications for the treatment of Obesity, but as already stated, results and patient compliance are rather mediocre.

A criterion for succesfull medical treatment of obesity is loss of 10% of weight in 6 months[71].

Medical treatment of obesity is under development and probably in the near future, the elucidation of the complex pathogenetic mechanisms that lead to obesity will yield powerful medications. But until then, intractable severe obesity treatment will rely mainly on surgery.

Part II: Surgical treatment of obesity

"...Those diseases,

which medicines do not cure,

the iron will...".

Hippocrates, *Aphorisms. VII-87*

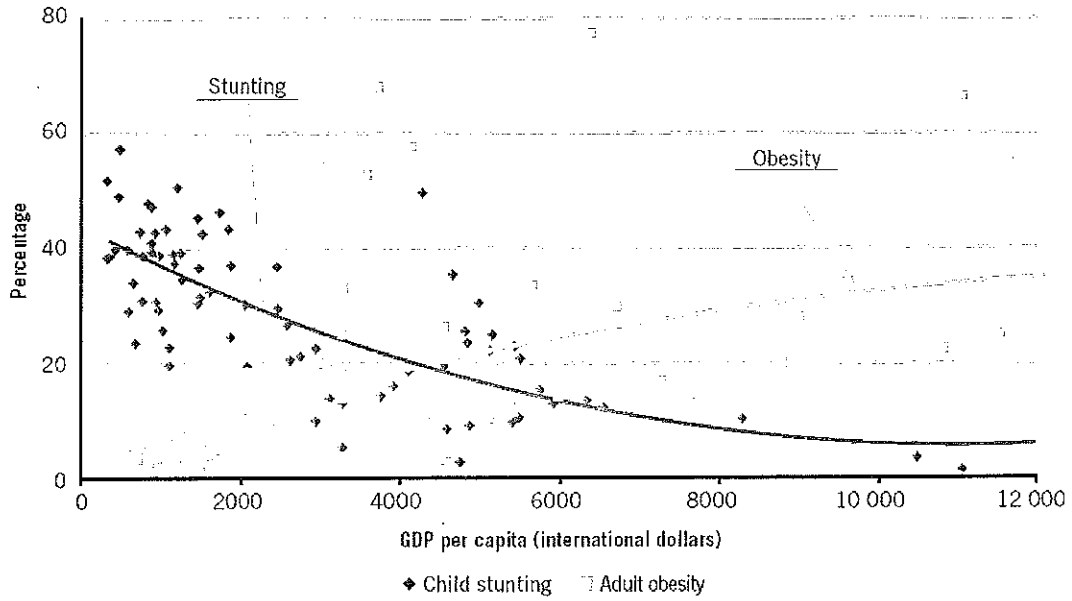
9. The evolution of bariatric surgery[72]:

In 1881 Theodore Billroth performed the first successful gastrectomy opening a new chapter in the evolution of surgery. Initially performed for cancer, gastric operations soon addressed functional problems, like peptic ulcer disease, pyloric stenosis and gastroesophageal reflux. Indeed, gastric surgery is one of the first surgical disciplines that intimately combined surgery and applied physiology.

On the other hand, after World War II industrialisation and food abundance marked the evolution of most western societies.

The global socioeconomic status in the western world increased, and with it of course, the per capita income also increased. This evolution is directly associated with the pandemic of obesity as depicted in fig 13 :

Fig 13: Adult obesity and child stunting variations in relation to per capita income. Source: WHO



The modern era was starting and a new plague started to spread. In the 50's and 60's the numbers of morbidly obese patients started to rise, and health care facilities found themselves unable to cope with obesity related problems, as some patients would not fit in beds, operation tables etc. The need for a weight reduction treatment became clear and medication or diets offered little help.

Surgery for obesity appeared in the early fifties, where the first iatrogenic short gut syndrome for the treatment of obesity appeared. It was a simple and radical solution performed in the superobese and without ethical revision boards or evidence based data, but then again it was the 50's. O tempora, o mores....

The first recorded jejunoileal bypass for the treatment of obesity was performed By Dr. Richard Varco in the United States. Varco divided and excluded a long intestinal loop, re-established continuity by anastomosing the proximal intestine with the ileum, and drained the excluded loop in the caecum. But Varco was preceded by a Swiss surgeon, named Victor Henriksson who performed a similar operation but Henriksson resected the excluded bowel making the procedure definitively irreversible.

Empiric treatment of obesity had started, but no reliable data were published and no audit existed to evaluate these procedures. Empiric treatment was soon replaced by knowledge based surgical procedures as scientific interest turned towards the physiology of nutrition and bowel function. The work of Kremen, Linner, and Nelson in 1953 entails the study of intestinal absorption in animal models and the authors published results of an intestinal malabsorptive procedure performed in an obese patient, based on their animal studies. This publication was the first publication in the history of bariatric surgery.

The late fifties were marked by many innovations in the bariatric surgery, but also with many complications as the idea of "controlled malabsorption" seemed elegant, but the golden standard was not determined. Many surgeons seeked the optimal balance between weight reduction with minimal denutrition side effects, and a variety of malabsorptive procedures were described. Many variations of the jejunoileal bypass were assessed and despite many complications weight reduction was achieved. Jejunoileal bypass was largely abandoned since, but it is the precursor of the modern malabsorptive bariatric operations.

In 1967 Mason and Ito introduced the combination of restriction and malabsorption by performing a proximal gastric division and loop jejunostomy on the fundic stomach. The second major step in bariatric step has been made, as surgeons realized that the component of restriction decreased the malabsorption requirements offering less nutritional complications. The gastric bypass procedure was born. Gastric bypass was refined by Alden, who suggested proximal stomach stapling without division and in 1977 Grifen et al introduced the first gastric bypass with Roux en Y jejunostomy. This last modification reduced tension and bile related stoma complications and was subsequently widely accepted by the international surgical community.

At the same period of rapid development of Gastric Bypass procedures, Mason was concerned with the side effects of such procedures and in an effort to create a surgical procedure for loosing weight without radical anatomic modifications he introduced with Printer in 1971 the first pure restrictive bariatric procedure. At the time, Mason proposed a horizontal partial stapling of the proximal stomach, leaving a conduit near the greater curvature. The idea was simple and ingenious, but long term results were rather disappointing. However the idea of pure restriction stayed and

many variations of the original Mason technique were introduced. In 1980, Mason presented his last variation of his technique, the famous Vertical Banded Gastroplasty This technique was further modified by Law in 1981 and by Eckhout et al in 1986 by the use of a silastic ring instead of a band, reducing band related complications and simplifying stapling techniques.

When Mason was working on restriction malabsorptive procedures were not widely accepted nor performed, until Professor Nicola Scopinaro of the University of Genoa presented the biliopancreatic diversion in 1979, also known as the Scopinaro Procedure. Scopinaro is considered the father of modern malabsorptive surgery as the biliopancreatic diversion is considered as probably the most effective bariatric operation till this day. Some of the technical details of the Scopinaro procedure will be discussed later.

More than ten years after Nicola Scopinaro described his new technique, the duodenal switch was introduced, initially by Marceau et al in 1993 and refined to its current form by Hess and Hess in 1998.

With the emergence of ingenious Pioneers like Mason and Scopinaro, the 80's were the evolutionary decade for Bariatric surgery, only to be followed by a yet more evolutionary decade of the 90's as laparoscopic surgery was also presenting a parallel progress and laparoscopic bariatric procedures started to emerge, offering the classic advantages of minimal invasive surgery to a group of patients with high co morbidity. Unfortunately most innovations are met with skepticism and bariatric surgery had its share of loath and contempt from non bariatric surgeons[73]. But with the perseverance of these pioneers and many more who followed, surgery for the obesity became recognized and respected globally.

Predictions that bariatric surgery will be abandoned not only were wrong, but as Winston Churchill once said: *"It is not the end, it is not even the beginning of the end, but it is, perhaps, the end of the beginning..."*

10. Main Bariatric procedures

"Wise temperance of the stomach is a door to all the virtues.

Restrain the stomach, and you will enter Paradise..."

Bishop Ignatius Brianchaninov (1807–1867)

Laparoscopic adjustable Gastric Banding, Roux en Y gastric bypass, Biliopancreatic diversion, Duodenal switch and the Vertical banded gastroplasty are the operations that managed to withstand time and clinical trials and constitute the vast majority of bariatric operations performed today (vide infra) In the present section a brief outline of these operations will de discussed.

10.1 Laparoscopic Adjustable Gastric Banding (LAGB)

Gastric banding is a modern mutation of the original vertical banded gastroplasty as Mason managed to prove that partitioning of the proximal stomach can indeed result in considerable and sustained weight loss. As we already said, the Mason technique was a revolution on the era of bariatric surgery, but although a lot less invasive than bypass procedures, it still required gastric stapling rendering reversibility difficult. Efforts to further simplify the technique finally resulted in the inflatable gastric banding technique first performed by Kuzmac et al in 1986[74]. The concomitant rapid evolution of laparoscopic surgery in combination with variations of the Kuzmac procedure, resulted in the modern adjustable gastric banding technique. as the first commercially available inflatable ring became commercially available in 1993 (INAMED Health).

A pure restrictive procedure, gastric banding consists of encircling the proximal stomach with an inflatable band, leaving a small gastric pouch of 15-30ml. The band circumference can be adjusted by "inflating" the balloon via a subcutaneous

port. To prevent it from slipping distally, the band is stabilized by over suturing the fundic part of the stomach.

Initially, gastric banding had a high rate of early complications and more specifically ring displacement and gastric prolapse through the ring. reported in up to 23% of patients. This was due to the high supra lesser omental approach of ring placement. In order to correct this serious complication the "pars flacida approach" was described with ring placement through the superior portion of the pars flacida, above the peritoneal reflection of the bursa omentalis[75].

The advantages of this technique are that it does not cause major anatomic modifications, its fairly easy reversibility and the fact that it is adjustable by means of its inflatable component.

10.2 Vertical Banded Gastroplasty (Mason Gastroplasty - VBG)

One of the first restrictive procedures ever performed, VBG has proven its self effective during the years. It consists of creating a small pouch of approximately 15 ml from the small curvature of the stomach with a vertical stapling technique. The outlet of the pouch is secured by a band to prevent dilatation. Silicone ring vertical banded gastroplasty is a successful variation of the classic Mason technique. Advantages of this technique rely on the creation of the small pouch limited by the staple line and the banded area. Disadvantages are that it requires stapling which tends to fail in long term in up to 30 – 35% of patients[76], although recent modern stapling techniques could reduce this complication down to 10%[77], that it is not adjustable and not readily reversible.

10.3 Roux en Y Gastric Bypass (RYGB)

This is a combination of restriction and malabsorption. A small gastric pouch of 10 – 30 ml is created by stapling and dividing the proximal stomach.. The small size of the gastric pouch creates the restrictive component. Drainage of the gastric pouch is accomplished by a gastrojejunostomy with a classic Roux en Y configuration. The length of the alimentary loop is usually 100 to 150 cm (ranging from 60 to 200 cm) depending on the weight of the patient and surgeon preference. Although a great number of these operations has been performed, there is yet to be a global consensus in the technical details of this operation, Thus according to surgeon experience various bypass procedures differ in the size of the gastric pouch, size of the gastrojejunostomy, use of a Fobi type ring to prevent pouch dilatation, length of intestinal limbs, antecolic vs. retrocolic placement of the alimentary limb and closure of mesenteric defects. A mathematic calculation of the combination of all these factors yields a number of 256 variations of the RYGB, using the afore mentioned parameters.

The powerful weight loosing mechanism of gastric bypass is due to combination of restriction and malabsorption. The overall result is decreased caloric intake which is achieved by a combination of the following mechanisms[78]:

- Anorexia: the small gastric pouch and the decreased rate of gastric emptying create a satiety feeling and in some cases aversion to food thus decreasing the desire to eat.
- Small gastric pouch: Fashioning a small gastric pouch restricts the capacity of food intake even in the absence of anorexia. The small pouch is considered a principal factor for RYGB success.

- Narrow stoma: A 12 mm stoma is considered the ideal pouch outlet, permitting slow gastric emptying and therefore greater period between meals.
- Dumping syndrome: Dumping is a complication of RYGB, but when moderate it is considered a convenient one, as patients avoid nutritients rich in glucose. However one must not forget that dumping syndrome can be a devastating complication in its extreme spectrum.
- Fat malabsorption: RYGB allows delayed mixed of food with the biliopancreatic juices, thus creating malabsorption of fat and fat soluble nutritients, decreasing caloric absorption.

These mechanisms are considered as the mediators of the weight reducing effects of RYGB, but the exact pathophysiologic neurohumoral pathways are yet to be fully elucidated.

A great advantage of this procedure is that flow is maintained through the "bypassed" limb, thus avoiding bacterial overgrowth related complications.

10.4 Biliopancreatic diversion (The Scopinaro procedure -BPD) and Duodenal switch

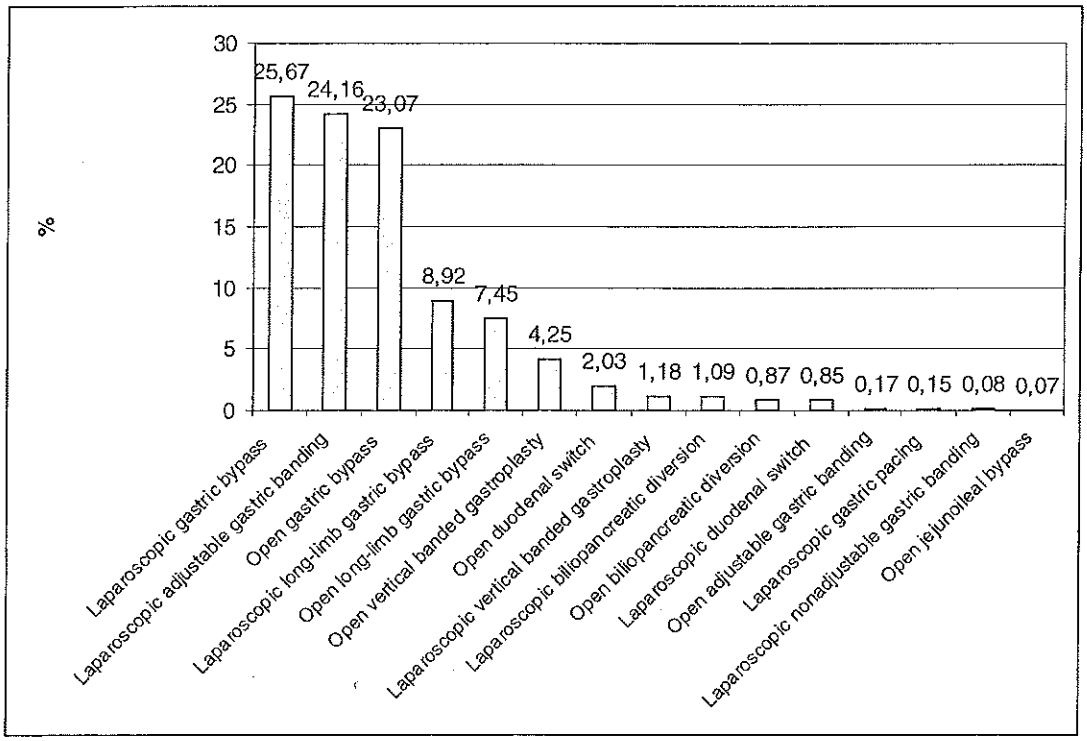
Although considered a malabsorptive bariatric operation one should not forget the restrictive component of this operation. It consists of a distal gastrectomy with the creation of a rather large pouch of 200 – 500 ml. Small bowel is divided 250 cm proximal to the ileocecal valve and it is anastomosed to the stomach remnant, thus forming the alimentary limb. The biliopancreatic limb is anastomosed 50 cm proximal to the ileocecal valve. The weight reducing mechanism of BDP is due to the delayed meeting of food with the biliopancreatic juices and malabsorption of fat and starch. Contrary to RYGB, in the Scopinaro procedures food will be mixed with the biliopancreatic fluid very distally, allowing only the 50 last cm of ileum to handle the absorption. This is the major advantage of this powerful weight reducing technique, but it is also the major disadvantage, as nutritional management becomes a lot more challenging.

The duodenal switch is a variation of the classic Scopinaro procedure. The differences are that instead of performing a classic distal gastrectomy, a vertical gastrectomy with stomach tubulisation is performed, and pylorus is preserved. The alimentary limb is connected with the proximal postpyloric duodenum in a terminoterminal fashion. Duodenal switch operation was born in 1993 in Canada and is gaining momentum in North America. Due to high fat diet in these areas, the biliopancreatic limb is connected 100 cm proximally to the ileocecal valve (instead of the 50 cm proposed by Scopinaro) in order to reduce adverse gastrointestinal and nutritional effects[79].

11. Current status of Bariatric surgery.

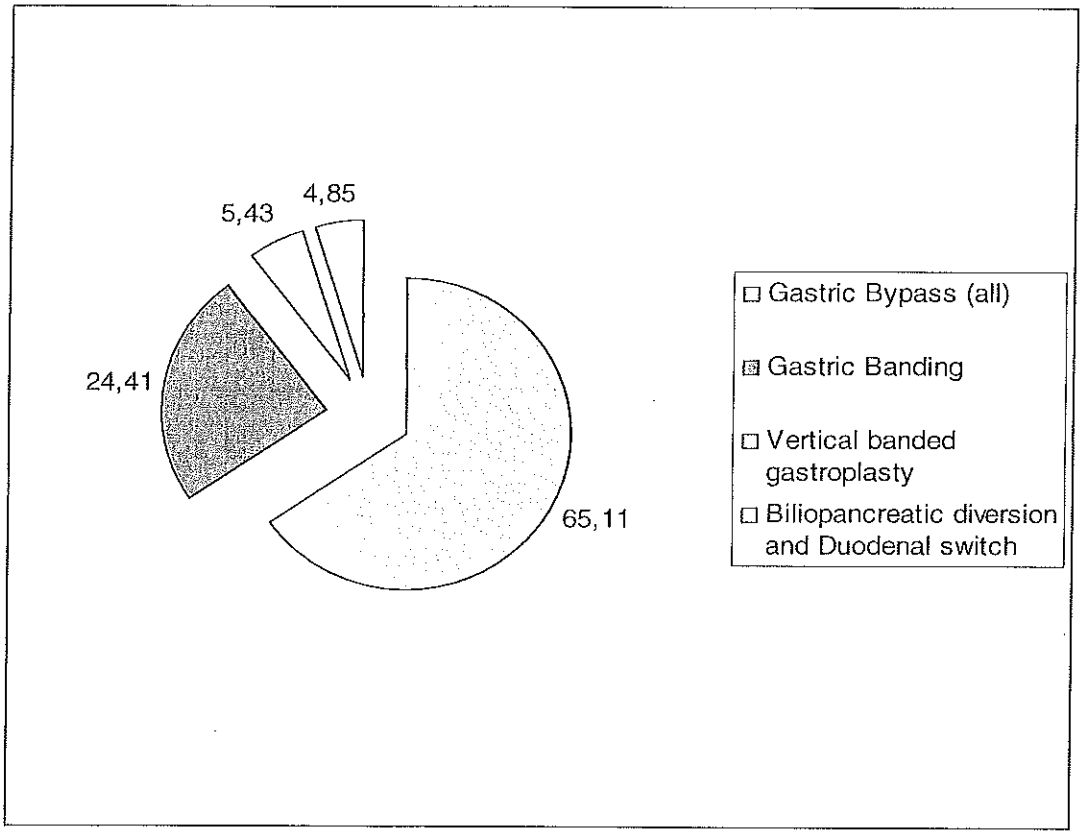
The aforementioned short historical review provides only a glimpse to the wave of innovation that striked the field of abdominal surgery as bariatrics became established. To date, more that 100 different operations for the treatment of obesity have been proposed[80], but the golden standard, the most frequently performed bariatric operations globally is laparoscopic adjustable gastric banding and Laparoscopic Roux en Y gastric bypass. Fig 14 shows the frequency of bariatric operation globally in 2003[81].

Fig 14 : % of Bariatric operations performed globally – Data from ref 81



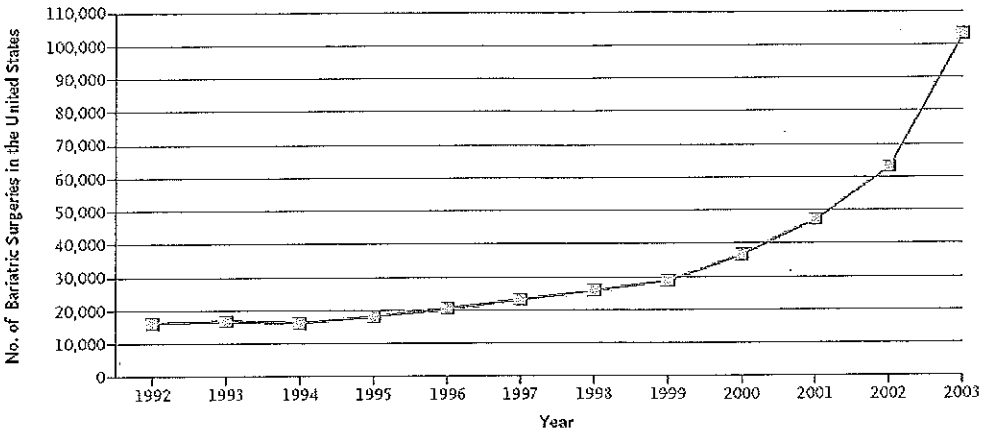
From a great variety of bariatric operations, Roux en Y gastric bypass and gastric banding have the lead in global bariatric practice. If we accumulate percentages of open and laparoscopic procedures, these two operations constitute almost 90% of bariatric operations performed (fig 15).

Fig 15 : % of Laparoscopic and open operations performed globally- Data from ref 81



The efficacy of these procedures, especially when they combined with minimal invasive techniques, is reflected by the significant increase in the number of operations performed yearly. In the United States alone, between 1998 and 2002, there was a 450% increase in the number of bariatric operations performed, a 144% increase in the number of American Society for Bariatric Surgery bariatric surgeons, and a 146% increase in the number of bariatric centers[82] (fig 16). Last year, 170.000 bariatric operations were performed in the United States. (ASBS press release 21/2/2006).

Fig 16 : Number of bariatric operations performed in the United States. Source: American Society of Bariatric Surgery



The present work will focus in the role of the two leading procedures for the treatment of obesity, Gastric banding and RYGB.

12: Indications for Bariatric surgical treatment.

Like all surgical procedures, bariatric surgery has its own share of complications which can be significant, especially in combination with obese patient co morbidity status and should not by anyway be considered the easy way out of obesity or a cosmetic procedure.

In order to protect patients and surgeons, the following guidelines have been established:

12.1 Bariatric surgery by who?

Guidelines for surgeons practicing bariatric surgery were established by the International Federation for the Surgery of Obesity (IFSO) at the 1997 Cancun statement[83] where the criteria for bariatric surgery qualifications were defined. According to this statement, prior to independently performing primary bariatric surgery, each surgeon should meet the following minimal standards:

1. be a fully-trained, qualified, certified general or gastrointestinal surgeon who has completed a recognized general/gastrointestinal surgery program;

2. has completed a preceptorship in all aspects of bariatric surgery including patient education, support groups, operative techniques and postoperative follow-up with an IFS0 or IFS0 Adhering Body-designated bariatric surgeon or one who has performed at least 200 bariatric surgical procedures and has 5 or more years experience in the field of bariatric surgery;

3. has received a written approval from his preceptor of his/her satisfactory bariatric surgical abilities;

4. maintains a well-informed, up-do-date knowledge of bariatrics and bariatric surgery literature such as contained in the journal Obesity Surgery;

5. has, or has applied for, membership in an Adhering Body of IFSO or, if no such national body is available to him or her, to IFSO directly;

6. has attended at least one meeting of IFSO or one of its Adhering Bodies or one of its bariatric surgery courses;

7. is personally committed to strongly encouraging the necessary education and life-long follow-up of his/her bariatric surgery patients;

8. performs bariatric surgery in institutions where he/she has made every reasonable effort to obtain equipment, facilities and support systems adequate for the comfort, safety and dignity of bariatric surgery patients.

12.2 Bariatric surgery for who?

The United States Massachusetts Department of Public Health issued via the National Guideline Clearinghouse in 2004 the guidelines for patient selection for surgical treatment of obesity[84]. According to these guidelines which are presented here, adult patients should benefit from bariatric surgical procedures when meeting the following criteria:

- BMI $\geq$ 40 kg/m^2, or BMI $\geq$ 35 kg/m^2 in association with major medical complications of obesity (e.g., cardiovascular disease, type 2 diabetes, sleep apnea)
- A well-informed and motivated patient
- A strong desire for substantial weight loss
- Failure of other nonsurgical approaches to long-term weight loss
- Acceptable operative risks

The Expert Panel strongly recommends preoperative and postoperative medical, nutritional, and behavioral/psychological care for weight loss surgery (WLS) patients. Recommendations in each area are listed below.

- *Behavioral/Psychological Care*

The Expert Panel recommends evaluation by a credentialed expert in psychology and behavior change, preferably a psychiatrist, psychologist, or social worker. He or she must be skilled at identifying psychological contraindications to WLS and potential barriers to success (e.g., inability to make needed behavior changes). They must be able to develop plans and implement treatments to address these barriers

Nutritional Care

The Expert Panel recommends preoperative education and counseling by a registered dietitian, with a well-defined diet progression after surgery. Early postoperative priority should be placed on maintenance of adequate hydration and protein intake . Blood levels of micronutrients should be assessed for deficiencies prior to surgery, 6 months after surgery, and at least annually thereafter. All patients should take a daily multivitamin and calcium supplement with added vitamin D. Thiamine supplementation should be considered for patients with persistent vomiting or poor intake. Prenatal multivitamins are an option for patients at risk of deficiencies in iron and/or folic acid. Regular use of additional iron supplements is also likely to minimize iron deficiency in at-risk patients. Patients who have had RYGB or malabsorptive procedures should be considered at risk for metabolic bone disease, and patients who have additional risk factors for metabolic bone disease should be assessed periodically after WLS.

- *Medical Care*

Physicians and nonphysician providers (e.g., nurses and physicians assistants) provide unique contributions to patient care; all should be considered important members of the multidisciplinary WLS treatment team. Extreme obesity is associated with several conditions known or suspected to increase operative risk. The following are recommendations for assessment and treatment for specific conditions:

- Obstructive sleep apnea (witnessed or daytime symptoms): The Expert Panel recommends preoperative assessment of patients with signs or symptoms of sleep apnea (e.g., increased neck circumference, daytime sleepiness, or other symptoms), as well as patients with hypertension, lower extremity edema, or cardiac dysfunction. There are insufficient data to recommend specific perioperative measures, although oxygen saturation monitoring appears prudent.
- Deep vein thrombosis/pulmonary embolism (DVT/PE): WLS patients are at high risk for venous thromboembolism (VTE) and should receive perioperative DVT/PE prophylaxis. Except where contraindicated, prophylaxis should be carried out via combined use of mechanical methods and anticoagulant strategies. Patients at particularly high risk for DVT/PE should be considered for preoperative inferior vena cava filter placement.
- Liver disease: Patients with unexplained elevations of hepatic transaminases should undergo preoperative evaluation for common etiologies of liver disease. Patients with preoperative or intraoperative evidence of fibrosis, cirrhosis, or hepatic dysfunction should undergo intraoperative liver biopsy. Those with evidence of insulin resistance should also be considered for

intraoperative liver biopsy. In cases where cirrhosis is found, decisions on whether to proceed with WLS should be made on a case-by-case basis; factors to consider include the overall health of the patient, the presence of gastric or intestinal varices or ascites, and the physical or histologic appearance of the liver.

- Smoking cessation: All patients who smoke cigarettes should be encouraged to quit, preferably at least 6 to 8 weeks prior to surgery. Use of nicotine replacements and/or bupropion may help minimize weight gain with smoking cessation. To reduce long-term health effects from smoking, patients should not resume tobacco use after surgery.
- Preoperative weight loss: All patients should be encouraged to lose weight prior to surgery. Those with BMI > 50 or comorbidities such as sleep apnea, type 2 diabetes, glucose intolerance, and hypertension should attempt to lose 5 to 10% of initial weight. Some patients (e.g., those already maintaining significant losses or taking medications that promote weight gain) may be unable to reduce weight prior to surgery. Decisions on whether to proceed with surgery in these patients should be made on a case-by-case basis given the limited data linking preoperative weight loss to safety or efficacy outcomes.
- Coronary Artery Disease (CAD): WLS patients with known or suspected CAD should receive perioperative beta blockers to reduce cardiovascular complications. Current guidelines from the American College of Cardiology and the American Heart Association recommend use of beta blockers prior to, during, and after surgery in patients with a history of CAD or with two or

more CAD risk factors, such as hypertension or high cholesterol (if use is not contraindicated).

Preoperative evaluation should be therefore conducted by a panel of experts, members of a multidisciplinary team of surgeons, endocrinologists, nutritionists and psychologists, in order to assure the strict and scientific application of the above recommendations

12.3 Expanded indications: Bariatric surgery for Adolescents

The obesity epidemic is currently roaming among the adolescent populations of developed countries, raising concerns for the treatment of this sensitive population. Currently there are no reliable large scale data that confirm the safety of bariatric procedures in adolescents, but the growing experience of bariatric surgery combined with the excellent results has created a positive trend towards this type of surgery in adolescents. Adolescents being considered for bariatric surgery should fulfill the following criteria[85]

- Have failed ≥6 months of available, organized attempts at weight management
- Have attained or nearly attained physiologic maturity
- Be very severely obese (BMI ≥40 kg/m^2) with serious obesity-related co morbidities or have a BMI of ≥50 kg/m^2 with less severe co morbidities
- Demonstrate commitment to comprehensive medical and psychologic evaluations both before and after surgery
- Agree to avoid pregnancy for at least 1 year postoperatively
- Be capable of and willing to adhere to nutritional guidelines postoperatively
- Provide informed assent to surgical treatment

- Demonstrate decisional capacity
- Have a supportive family environment

Needless to say that this group of patients should be closely followed postoperatively by highly specialized multidisciplinary teams in order to assure optimal nutritional support.

Bariatric surgery is currently performed in adolescents[86] and the need of reliable high volume data is evident, as controversy does exist[87] and there is no established evidence-based consensus on the indications and the techniques performed.

13. Complications of Bariatric surgery

Bariatric surgery is abdominal surgery in a patient group that by definition present a high risk, as obesity is intimately related with significant co morbidities.

Classic abdominal surgery complications may take big proportions in the obese subjects and surgeon high degree of suspicion and prompt management is essential in the postoperatory follow up.

Complications common to all bariatric procedures are the "classic" abdominal surgery complications like bleeding, wound infection, intraabdominal infection, wound dehiscence, incisional hernias, splenic injuries, thromboembolic events, acute post operatory obstructive ileus, pulmonary atelectasis, pneumonia and anesthesia related complications. Male gender and a BMI over 50 are considered as independed risk factors for an increased perioperative morbidity.

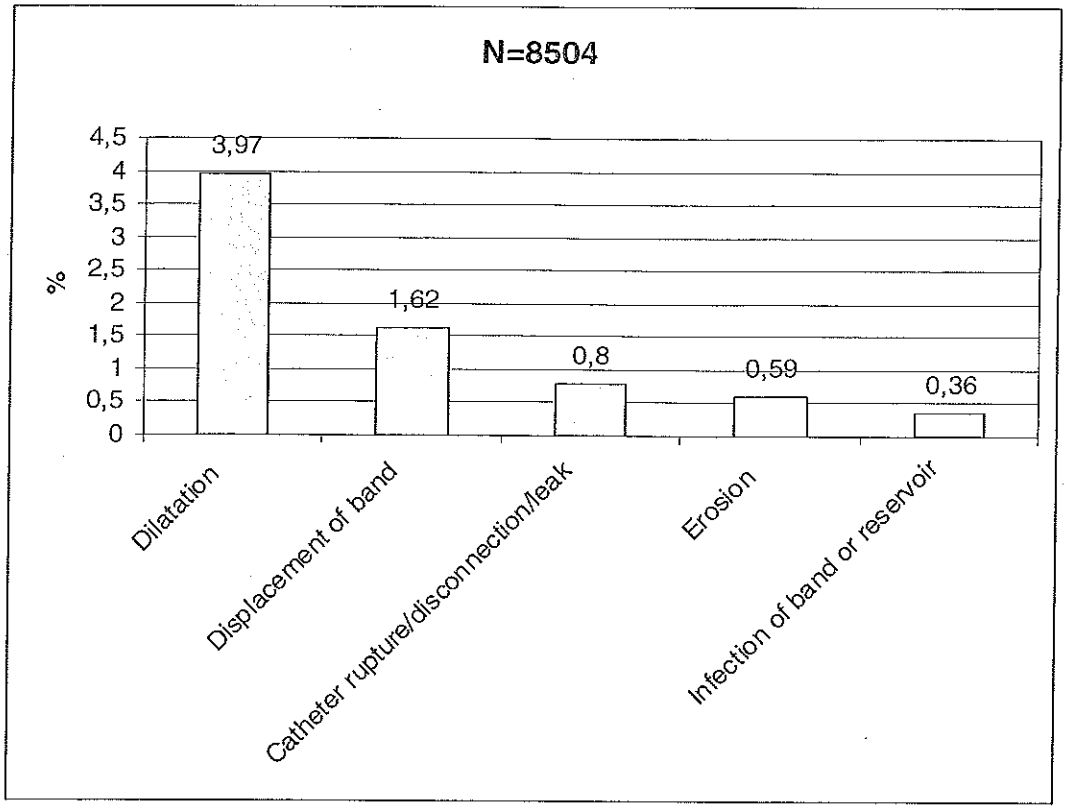
Gastroesophageal reflux is an adverse effect of both RYGB and LAGB, estimated to occur in 10.9% and 4.7% of patients respectively.

Vomiting after bariatric procedures is relatively common and its incidence is currently estimated at 15,7% for RYGB and 2.5% in LAGB.

Open procedures have significantly more wound related complications with overall incidence estimated at 11.4% as opposed to 2.3% for laparoscopic procedures.

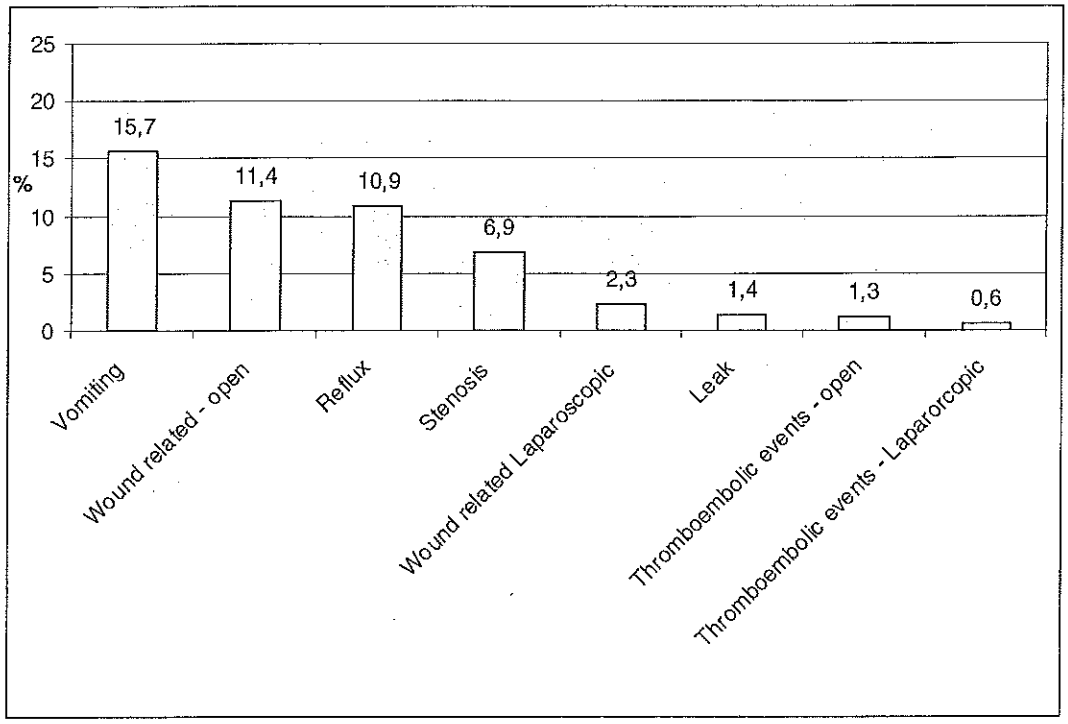
Laparoscopic adjustable gastric banding specific complications include band slippage, erosion of the band into the stomach, pouch or oesophageal dilatation, oesophageal injury, port site infections, dysphagia and mechanical problems related to the adjustable apparatus assembly, like balloon leaks or tube fractures (Fig. 17)

Fig 17 : Common complications of gastric banding: Data from the ASERNIP report[88]



RYGB specific complications (fig 18) are staple line disruption, anastomotic leaks, internal hernias, acute gastric dilatation, stomal stenosis, marginal ulcers, dumping syndrome and nutritional deficiencies like vitamin B12 and lipid soluble vitamin deficiency which can be observed in up to 40% of patients[91]. Compared with open procedures, laparoscopic gastric bypass has a higher rate of intraabdominal complications, but offers a lowers rate of wound complications, a shorter hospitalisation and a higher patient comfort.

Fig 18 : RYGB complications. Data from the Agency for Healthcare Research and Quality U.S. Department of Health and Human Services[89]



Until recently, there was no comprehensive registry for reporting these complications and data analysis is extremely difficult as reports vary according surgeon experience and technique used. Postoperative mortality is reported from as low as 0.1% to 2%[90] and morbidity is estimated at 5% for both procedures.[91] RYGB being a more complex a challenging procedure, has a higher morbidity than LAGB. Differences in the incidence of complications across studies is considerable and it is thought to be mainly due to operator related factors. It has been shown than experienced high volume surgeons are confronted with fewer complications.

A special mention is warranted concerning anastomotic leaks following bariatric surgery, which is a devastating complication. *Jammerecke,* the angle of grief, a term first used by Theodore Billroth to describe anastomotic angle leaks, is one of the most feared complications up to date. Obese patients in the immediate post operative period do not usually present with generalised peritonitis and anastomotic

leak can have a quite indolent presentation. High degree of suspicion is extremely important in these cases, and a patient with a persistent non explained tachycardia of >120 bpm and fever, should be considered to have an anastomotic leak unless proven otherwise. Prompt surgical revision is the treatment of choice for anastomotic leaks, although some reports support conservative treatment for well drained small leaks. The leak rate after laparoscopic gastric bypass is approximately 2.5% in most series, and the mortality risk from this complication is approximately 0.3%.[71] However data vary greatly from 0-5% probably signifying the difference between surgeon experience and anastomotic technique.

Tachycardia in the postoperative course after a bariatric procedure is indeed an ominous sign warranting immediate clinical evaluation. As Mason said: *"A sustained pulse higher than 120 /min requires the nurse to notify the surgeon in order to determine the cause before the sun sets (or rises). Otherwise, the patient may die from acute gastric dilatation, acute afferent loop syndrome or peritonitis."*[92]

Failure to loose weight is a multifactorial complication of RYGB and it can be due to a large pouch (>30 cc) or pouch dilatation, a large or dilated stoma (>14 mm), staple line failure, and idiosyncratic or non compliance patient factors.

An interesting complication of RYGB procedures is the appearance of endogenous hyperinsulinemic hypoglycaemia which can be severe. There are many theories trying to explain this phenomenon, and current concepts are in favour of the phenomenon of nesidioblastosis[93] (from the Greek nesos which means island and blastos which mean sprouting) following gastric bypass. Nesidioblastosis is defined as the hypertophy of b-cell islets and is thought to be the main mechanism responsible for hyperinsulinemic status after gastric bypass. The exact cause of nesidioblastosis is unknown but theories are in favour of b-cell hypertophy as a result of altered gut

hormone secretion due to the anatomic modifications of a gastric bypass. Whatever the cause, hyperinsulinemic hypoglycaemia should be in the differential diagnosis of postprandial hypoglycaemic symptoms which should not be readily attributed to the dumping syndrome. This potentially devastating complication is probably the extreme spectrum of a promising side effect of Gastric Bypass, because it is considered as the main mechanism of diabetes reversal, as more than 80% of patients present with resolution of type II diabetes weeks or even days after RYGB.[94]

A subject of increasing concern in bariatric surgery is the relationship between Bariatric surgical operations – especially RYGB- and gastric cancer. It is believed that an operated stomach predisposes to an increased risk of gastric cancer. This observation dates as back as the year 1919, when Balfour has published the first paper linking gastric surgery for benign disease with an increased incidence of gastric cancer[95]. Since then, a great number of papers addressing this matter have been published and although the findings were relatively inconsistent between the various reports, the common conclusion was that gastric surgery, especially Billroth type II, does indeed predispose to late gastric cancer, especially 20 years post operatively.

Researchers have also demonstrated that the peptic ulcer disease itself is not responsible for post gastrectomy gastric cancers, but rather the intestinogastric anastomosis is the factor to blame for the increased incidence of malignant transformation of the gastric mucosa. Mechanisms mediating this alarming possibility are thought to be mediated by intestinal juice reflux into the stomach which is shown to provoke gastric mucosal metaplastic changes in animal models but also in humans. In addition to this, nitrosamine increased synthesis due to intestinal flora overgrowth adds to the increased cancer risk, as nitrosamines are known to be cancerogenic.

After the discovery of helicobacter pylori and the proton pump inhibitors, peptic ulcer disease became a non surgical disease with surgery reserved for complications, and the number of gastrectomies for gastric or duodenal ulcer has drastically declined. However, with the increasing popularity of RYGB for the treatment of obesity, patients carrying Billroth II type gastrojejunal anastomoses are increasing. Up to date, there are no reliable large scale epidemiologic data linking bariatric surgery to gastric cancer. However sporadic case reports do exist[96,97,98], and an increased degree of suspicion should be maintained on the follow up of bariatric patients. In the July 2006 issue of obesity surgery alone, 3 articles are published with case reports of gastric cancer following bariatric surgery.[99, 100, 101] A study by Kuwano in 1988 confirms gastric mucosal metaplastic changes following horizontal gastroplasty in animal models[102], and its findings are confirmed by the work of Negri[103]. As far as gastric remnant mucosal changes are concerned, the risk of cancer after RYGB is unknown, but theoretically it could be exposed to an increased contact of biliopancreatic juices that are shown to be cancerogenic.[104]

Bibliographic data cannot support a clear connection between bariatric surgery and gastric cancer. However, the mucosal changes observed in the gastric pouch after VBG or gastric banding and in both the proximal and distal stomach after RYGB could suggest that post bariatric surgery patients could indeed comprise a high risk population for late cancer development, and an organised international bariatric registry for reporting such cases should be considered in order to evaluate this potentially disastrous complication.

14. Results of Bariatric surgery

In 1995 Pories at al have published an article titled: "Who would have thought it? an operation proves to be the most effective therapy for adult-onset diabetes mellitus[94]". This article would mark the evolution of bariatric surgery, as the international scientific community was presented with revolutionary data confirming the unexpected and profound effects of bariatric surgery on obesity related co morbid conditions. For the first time it was realised that bariatric procedures were not simply weight reduction procedures but caused complex metabolic alterations that were advantageous for the patients.

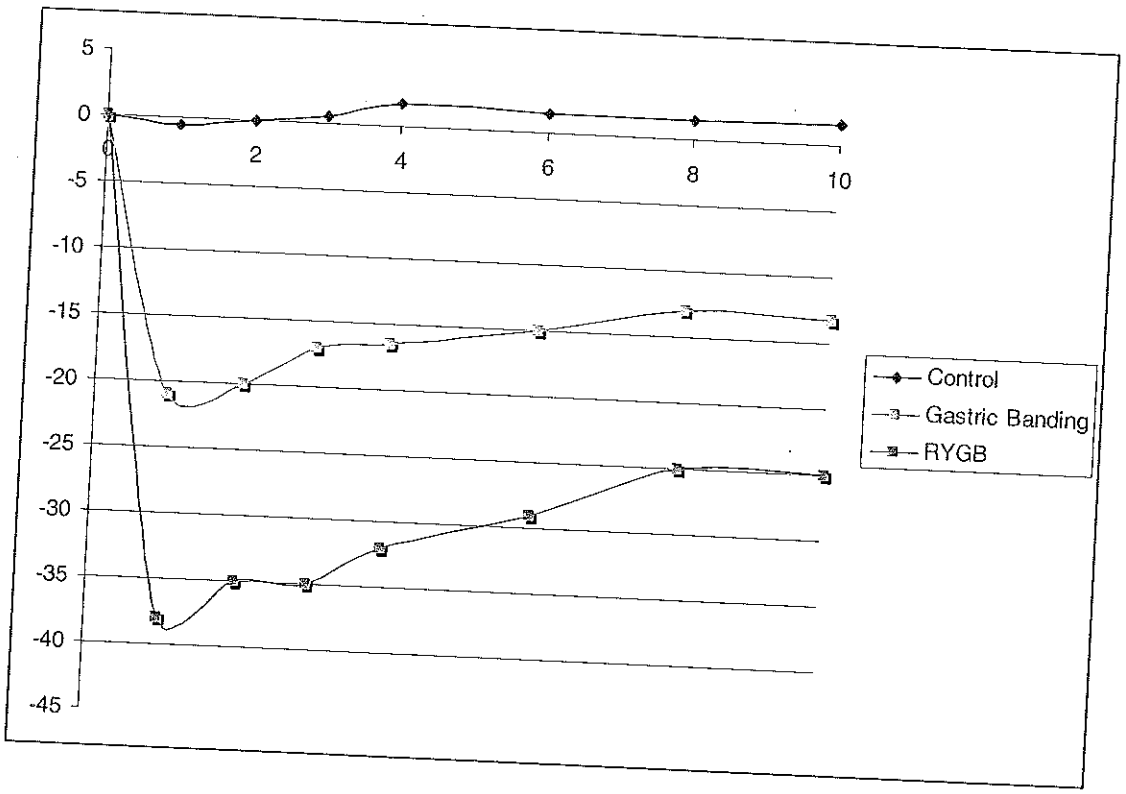
The Pories article triggered a wide response and many researchers started to analyse long term bariatric surgery results. The conclusions drawn from this research show that bariatric surgery improves quality of life, Type II diabetes, cardiovascular risk factors and sleep apnea.

Through the years, as experience increased and learning curves have levelled, bariatric surgery has proved to be an effective consistent and reliable surgical solution to morbid obesity.

Recently the Swedish Obese Subjects Scientific Study Group (SOS) has published results of bariatric surgery procedures with a follow up as long as ten years. According to this study published in the New England Journal of Medicine in December 2004, surgery appears to be a viable option for the treatment of obesity, as it results in considerable and sustained weight loss, improved quality of life and a decrease of several obesity related cardiovascular risk factors.

As far as RYGB and Gastric banding are concerned, this study has demonstrated that both procedures are reliable methods for loosing weight and for sustaining a lower BMI, as illustrated in Fig 19:

Fig 19: Results of bariatric surgery: In the horizontal axis the years after the operation and in the vertical axis the percentage of weight alteration over time. Control subjects had medical treatment.



Sustained weight loss has proved to be beneficial not only in the body image issues but also in the evolution of cardiovascular risk factors, as hypertriglyceridemia, diabetes, and hyperuricemia – but not hypercholesterolemia- seem to be lower in the group of patients treated with surgery at two and at ten years after their operation. Between Gastric Banding and RYGB the second offers more significant decrease in weight and cardiovascular risk factors, being a more complex operation, probably through altered gut to brain signaling mechanisms.

Hypertension improves after bariatric surgery in 60 to 83% of patients[105], and improvement seems to be unrelated to the type of the procedure performed and it is related to the percentage of weight loss[106].

The profound effect of bariatric surgery on type II diabetes is one of its major advantages as it results in up to 98% decrease in the incidence of diabetes and 90% in the incidence of insulin resistance. All bariatric operations improve type II diabetes, but the malabsorptive component of an operation seems to be directly involved in the diabetes outcome. Consequently diabetes improvement is reported at 98.7% for biliopancreatic diversion or duodenal switch, 83.7% for gastric bypass, 71.6% for gastroplasty, and 47.9% for gastric banding[94,107,108]. These differences reflect the implication of gut hormone regulation mechanisms in addition to weight loss that mediate the metabolic profile alteration of bariatric surgery patients.

Sleep apnea is also dramatically improved after bariatric surgery and improvement is reported as hi as 80%[109, 110].

Idiopathic intracranial Hypertension (pseudotumor cerebri), a syndrome of increased intracranial pressure in absence of space occupying cerebral lesions or hydrocephalus has a causal relationship with Obesity, and it is known that marked weight loss in these patients results in resolution of this condition[111].

As far as the mortality is concerned, it was estimated that bariatric surgery offers an 89% decrease[112] in the all cause mortality.

Adjustable gastric banding techniques have the major advantage of being a lot less aggressive than RYGB, but it is less powerful than gastric bypass and a recent article in Obesity Surgery Journal[113] has shown that long term results have a tendency to worsen over time and that complications rise 3-7% every year after surgery. This article raises questions in the long term efficacy of Gastric Banding and it stresses the need for long term results studies with extended and reliable follow up. As far as the superobese patients are concerned, RYGB is the procedure of choice, as it has been

shown that LAGB is associated with higher failure rates, patient dissatisfaction, reoperations and comorbidity reduction than RYGB in these patients[114].

Given the relatively poor long term bibliographic data, the choice of the type of bariatric operation that should performed should be made very carefully, after extensive discussion between a well informed and motivated patient and an experienced bariatric surgeon.

The overall results of bariatric surgery up to date are encouraging however and they confirm the favorable impact of the surgical treatment on the obesity pandemic.

Obesity surgery does not come cheap, as hospital fees, costs of equipment, surgeon fees and insurance economic burden is a non negligible factor in the treatment policies of a population that is constantly increasing. But up to date, the vast majority of cost effectiveness analyses have shown that the costs of the surgical treatment of obesity, even though considerable, result in an overall beneficial economic balance 4 years after surgery, as the economic burden for treating obesity related problems outweigh the actual cost of bariatric surgery just 4 years after the operation.[115, 116]. Although initially bariatric surgery was treated with hostility by insurance companies and policy makers, it is now clear that the reduction of related co morbidities, the improvement in quality of life and patient productivity after this type of surgery, makes it a cost effective method for the treatment of obesity.

15. DISCUSSION AND CONCLUSIONS

Most of the arguments for the role of bariatric surgery in confronting obesity have been analytically discussed in the second part of the present work. There for, in this final chapter we will be staying with general discussion points leading to conclusions.

Obesity is a chronic debilitating disease that is taking pandemic proportions worldwide. Conventional treatments with behavioral modification, diet, exercise and medication have disappointing results and seem to be unable to control the disease. Surgery on the other hand, is gradually gaining momentum as a treatment of choice for refractory obesity. Technological advancement in stapling techniques, surgeon experience and the evolution of laparoscopic surgery, have contributed to the rapid and favorable evolution of bariatric surgery, which is today the only effective treatment of morbid obesity.

Restricting food intake or creating calorie malabsorption (or the combination of both) seem simple logical solutions for weight reduction, however, the scientific community was surprised to discover that bariatric operations were not only promoting weight loss but were also able to cure type II diabetes and to significantly reduce obesity related co morbidities, offering a considerable amelioration of patient quality of life.

Currently, bariatric surgery is a recognized and respected branch of general surgery that is constantly evolving. Review boards and bariatric associations are forming guidelines that will help doctors and surgeons to properly select candidates for surgical treatment and design the appropriate procedure. However, this is only the beginning (or the end of the beginning) and the journey will be long. As bariatric surgery gains momentum, so does its commercial value and strict adherence to

guidelines and indications should be thoroughly controlled and respected. Considering bariatric surgery as an aesthetic procedure would be disastrous for patients, surgeons and third party payers. Bariatric surgery is there to help seriously ill people to deal with a severe disease, not to encourage gluttony, sloth and abuse.

Finally, as Dr. Alfred Black said: "*it usually requires a considerable time to determine with certainty the virtues of a new method of treatment and usually still longer to ascertain the harmful effects*" Long term bariatric surgery outcomes are yet to be determined and an international registry for long term complications should exist and be thoroughly respected by every bariatric surgeon. Till the present day, the "risk versus benefit" doctrine favors bariatric surgery for the morbidly obese and surgery is indeed the treatment of choice for those patients.

But the universal doctrine, the ubiquitous dogma that should govern the surgical decision making process, both for experienced bariatric surgeons and for graduating rookies like the author, should be the words of Hippocrates:

"Above all, do no harm…".

ABBREVIATIONS

- **ASBS:** American Society of Bariatric Surgery
- **ASERNIP-S:** Australian Safety and Efficacy Register of New Interventional Procedures - Surgical
- **BMI:** Body Mass Index
- **BPD:** Bilio-Pancreatic Diversion
- **BPM:** Beats Per Minute
- **CAD:** Coronary Artery Disease
- **CDC:** Center of Disease Control
- **DVT:** Deep Venous Thrombosis
- **GDP:** Gross Domestic Product
- **GERD:** Gastro-Esophageal Reflux Diseases
- **IFSO:** International Federation for the Surgery of Obesity
- **LAGB:** Laparoscopic Adjustable Gastric Banding
- **NAFLD:** Non Alcoholic Fatty Liver Diseases
- **OECD:** Organization for the Economic Cooperation and Development
- **PE:** Pulmonary Embolism
- **QOL:** Quality Of Life
- **RYGB :** Roux en Y Gastric Bypass
- **SF-36:** 36-item short-form constructed to survey health status in the Medical Outcomes Study
- **VBG:** Vertical Banded Gastroplasty
- **VTE:** Venous Thrombo-Embolism
- **WHO:** World Health Organization
- **WLS:** Weight Loss Surgery

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Winged Victory of Samothrace
220-190 BCE
Hellenistic period – Marble
Louvre, Paris