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Review Article

Management of Excess Adiposity

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Abstract

The adipose tissue is the largest endocrine organ in humans, mainly located beneath the skin (subcutaneous adipose tissue) but also in other areas (e.g., visceral adipose tissue and ectopic adipose tissue). Excess adiposity is defined as the expansion of adipose tissue (e.g., hypertrophy and hyperplasia) leading to overweight/obesity and related comorbidities. Obesity is a major health problem worldwide inflicting high cost to the society. Management of excess adiposity requires multidisciplinary approaches including lifestyle (e.g., diet, exercise, and behavioral change), food supplements, drugs, medical devices, gut microbiome modulation, body contouring, and bariatric surgery. Long-term weight maintenance remains a challenging goal in most cases.

Keywords: Adipose tissue; Excess adiposity; Overweight; Obesity; Management; Lifestyle; Drug; Medical device; Surgery

Abbreviations: AZ: Arizona; BMI: Body Mass Index; EDC: Endocrine-Disrupting Chemical; e.g.: Exempli Gratia; kg: Kilogram; LAGB®: Lap-Band® Adjustable Gastric Banding; LLC: Limited Liability Company; m: Meter; MD: Medical Doctor; mL: Milliliter; TPS®: TransPyloric Shuttle®; USA: United States of America

Introduction

The adipose tissue is the largest endocrine organ in humans. It is mainly located beneath the skin (subcutaneous adipose tissue) but also in other areas (e.g., visceral adipose tissue and ectopic adipose tissue) [1-5]. It plays a vital role in the survival of humans. In addition to its mechanical and storage properties, adipose tissue has important metabolic and endocrine functions.

Excess adiposity is defined as the expansion of adipose tissue (e.g., hypertrophy and hyperplasia) leading to overweight/obesity and subsequent morbidity and mortality [6-8]. Obesity is a major health problem worldwide inflicting high cost to the society [9,10].

Management of excess adiposity requires multidisciplinary approaches including lifestyle (e.g., diet, exercise, and behavioral change), food supplements, drugs, medical devices, gut microbiome modulation, body contouring, and bariatric surgery [6,11-24].

Normal Adipose Tissue

The adipose tissue is the largest endocrine organ in humans (Figure 1). In normal young adults, the adipose tissue represents 8 to 19% of total body mass in men and 21 to 32% in women. It contains adipocytes, connective tissue, nerve tissue, vascular cells, and immune cells [2,5]. There are three types of adipose tissue, white adipose tissue (the predominant type), brown adipose tissue, and beige adipose tissue (new classification) [1-5].

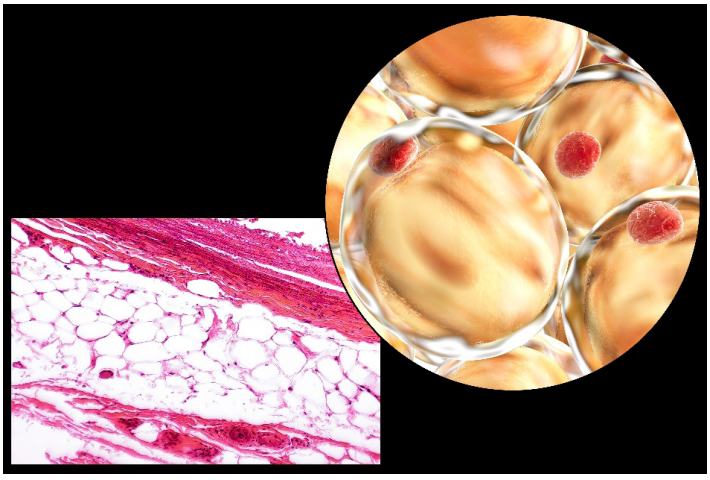

Figure 1: The adipose tissue is the largest endocrine organ in humans. Copyright katerynakon (Kateryna Kon)/Depositphotos Inc.

Distribution

White Adipose Tissue

The white adipose tissue is located beneath the skin (subcutaneous adipose tissue) and other areas (e.g., visceral adipose tissue and ectopic adipose tissue) [1-5,25]. The subcutaneous white adipose tissue is the most abundant component of adipose tissue in lean subjects, representing approximately 80% of total adipose tissue (Figure 2). The visceral white adipose tissue is localized around several internal organs (e.g., epicardial adipose tissue). The ectopic white adipose tissue is localized within internal organs (e.g., liver and pancreas). These adipose tissues represent 6 to 20% of total adipose tissue.

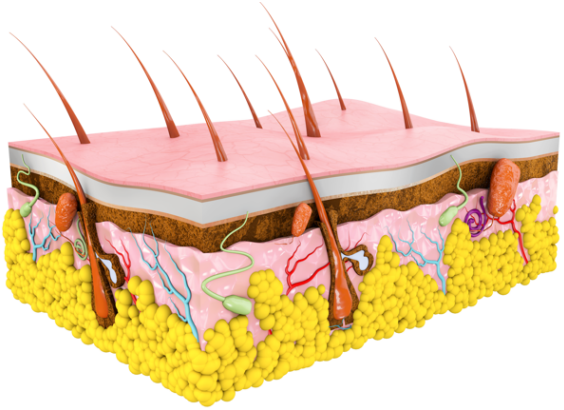

Figure 2: The subcutaneous white adipose tissue represents approximately 80% of total adipose tissue in lean subjects. Copyright tussiksmail.gmail.com (Victor Josan)/Depositphotos Inc.

Brown Adipose Tissue

The brown adipose tissue is located primarily in the cervical, axillary, and paraspinal regions [1,2,5,25]. Brown adipose tissue represents approximately 1-2% of total adipose tissue [5].

Beige Adipose Tissue

The beige adipose tissue represents a new classification. It has been described as the presence of brown adipocytes within white adipose tissue [4,5].

Regulation

The white, brown, and beige adipose tissues are innervated by the sympathetic nervous system whose activation is necessary for the functions of different adipose tissues [4]. The metabolism of adipose tissue is also influenced by several hormones including growth hormone, leptin, insulin, and cortisol (non-exhaustive list).

Role

The white adipose tissue plays a vital role in the survival of humans. It is involved in heat insulation, dermal infection barrier, mechanical protection (cushion), and storage of excess energy as triglycerides. It is a highly active metabolic and endocrine organ involved in the production of adipocytokines (e.g., leptin, adiponectin, resistin, omentin, interleukin 6, and tumor necrosis factor alpha) which act at both local (autocrine, paracrine) and systemic (endocrine) levels, affecting energy homeostasis, insulin sensitivity, and neuroendocrine, cardiovascular, and immune functions (Figure 3) [1,2,4,5,25].

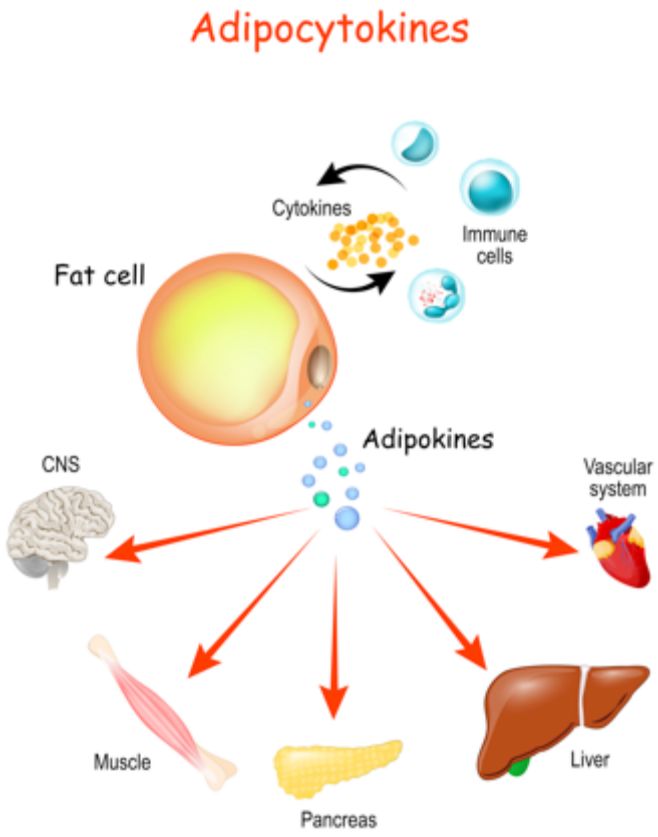

Figure 3. The white adipose tissue produces several factors called adipocytokines with autocrine, paracrine, and endocrine functions. Copyright edesignua (Tetiana Zhabska)/Depositphotos Inc.

The brown adipose tissue is involved in thermoregulation. It transfers energy from food into heat [1,4,5]. Although the mass of the brown adipose is relatively small, its contribution to metabolic health is important. It produces adipocytokines and exclusively secretes molecules called batokines (e.g., fibroblast growth factor). The exact role of the beige adipose tissue has yet to be determined [4,5].

Physiological Variations

Age

With aging, adipose tissue undergoes significant changes in mass, distribution, composition, and secretory profile due to chronic positive calorie balance, reduced physical activity, and lower basal metabolic rate [1,2,4,25,26]. White adipose tissue mass increases, peaks around 65-70 years, but decreases in very old ages. The increase in visceral adipose tissue mass is more pronounced in women [26]. There is an increase in the levels of most adipocytokines (e.g., leptin, adiponectin, resistin, interleukin 6, and tumor necrosis factor alpha) with aging [25]. Elevated levels of pro-inflammatory adipocytokines (e.g., interleukin 6 and tumor necrosis factor alpha) can negatively impact aging and lifespan by promoting chronic diseases (e.g., obesity, type 2 diabetes, and ischemic heart disease). In contrast, elevated levels of adiponectin, an anti-inflammatory adipocytokine, can be beneficial and responsible for the favorable metabolic phenotype of centenarians, explaining their extended longevity. Brown adipose tissue and beige adipose tissue masses also decrease with aging.

Gender

Overall, men have a lower total body adipose tissue percentage than premenopausal women but have more adipose tissue in the abdominal subcutaneous and visceral areas [3,25].

Disorders of Adipose Tissue

Disorders of adipose tissue affect mainly white adipose tissue. They include accumulation of lipophilic endocrine-disrupting chemicals (EDCs) responsible for several medical disorders, excess adiposity (e.g., hypertrophy and hyperplasia) leading to overweight/obesity and related comorbidities, and deficient adiposity (e.g., lipodystrophies).

Accumulation of EDCs

EDCs are a heterogenous group of exogenous chemicals or chemical mixtures that interfere with the action of hormones. EDCs are present in a variety of products [27]. The majority of EDCs are highly lipophilic, stored in adipose tissue, and resistant to degradation. The chronic release of EDCs stored in adipose tissue can promote several medical disorders including diabetes, obesity, nonalcoholic fatty liver disease, infertility, and cancers (non-exhaustive list) [27].

Excess Adiposity

The body mass index (BMI) is used as a surrogate marker for adipose tissue mass and for defining overweight/obesity [6]. Overweight is defined as a BMI ≥ 25 and < 30 kg/m^2 and obesity as a BMI ≥ 30 kg/m^2. In some Asian countries (e.g., China and Japan), the thresholds to define overweight and obesity are lower. The BMI may not be an accurate tool to assess obesity since it does not take body composition into account.

The expansion of the adipose tissue occurs when energy intake exceeds energy expenditure. The adipose tissue can expand by either hypertrophy (increase in the size of adipocytes) or hyperplasia (increase in the number of adipocytes). The excess adiposity leads to overweight/obesity. The subcutaneous white adipose tissue acts as a buffer for excess lipid storage (Figure 4). When this storage capacity is exceeded due to limited hypertrophy or hyperplasia, the excess fat accumulates outside of the subcutaneous area, causing visceral obesity. Obesity is a major health problem worldwide. Its prevalence has doubled in more than 70 countries since 1980 [8]. The number of adult subjects with obesity is around 650 million worldwide.

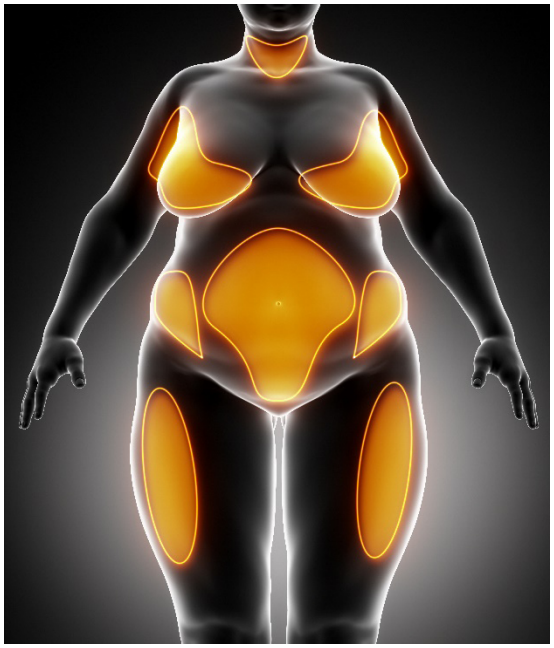

Figure 4: Excess fat deposits in the subcutaneous areas. Copyright CLIPAREA (Peter Lecko)/Depositphotos Inc.

Causes

The pathogenesis of excess adiposity leading to obesity is complex. Several factors can contribute (e.g., genetic, sociocultural, behavioral, environmental, and medical factors) (non-exhaustive list) [6].

Consequences

Excess adiposity leading to obesity is associated with increased morbidity/mortality and high cost for the society [6-10]. Multiple organs and systems are impacted by obesity (Figure 5) (Table 1). Visceral obesity is strongly associated with

cardiometabolic risk factors, especially in women [28]. Nearly 4 million subjects die each year from the consequences of obesity. People with obesity spend approximately 30% more on medical care than people without obesity. The annual worldwide cost of obesity is more than $2 trillion.

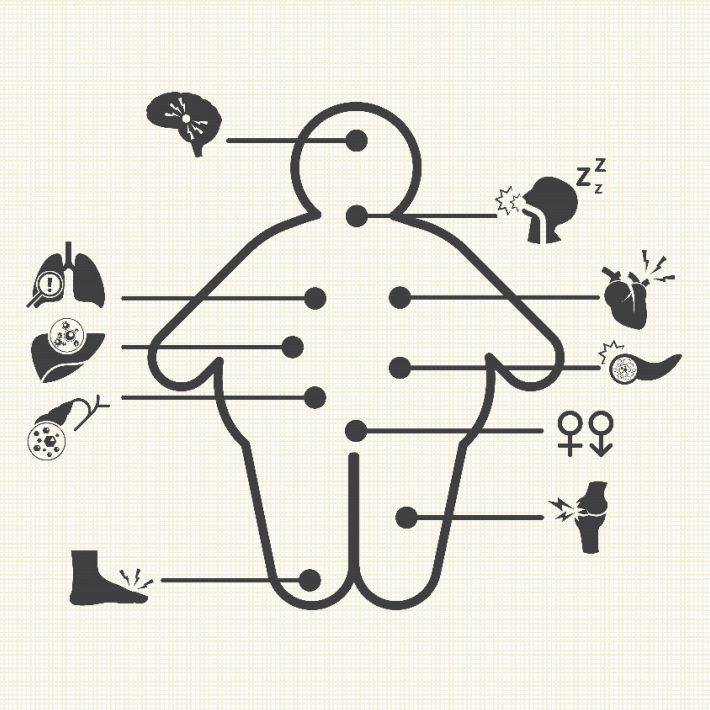

Figure 5: Organs impacted by obesity (non-exhaustive list). Copyright Kittichai (Kittichai Songprakob)/Depositphotos Inc.

Impacted Systems	Comorbidities
Endocrine/Metabolic	Prediabetes, Type 2 diabetes, Early puberty, Infertility, Dyslipidemia, Gout
Cardiovascular	Myocardial infarction, Stroke, Atrial fibrillation, Hypertension, Venous thromboembolism
Respiratory	Sleep apnea, Asthma
Gastrointestinal	Nonalcoholic fatty liver disease, Gallbladder disease
Musculoskeletal	Osteoarthritis
Oncological	Breast cancer, Endometrial cancer, Colorectal cancer
Neurological	Chronic pain
Psychiatric	Depression

Table 1: Systems impacted by obesity and the resulting comorbidities (non-exhaustive list).

Management

In addition to preventive measures, management of excess adiposity requires multidisciplinary approaches including lifestyle (e.g., diet, exercise, and behavioral change), food supplements, drugs, medical devices, gut microbiome modulation, body contouring, and bariatric surgery (Table 2) [6,11-24].

Tools	Description
Lifestyle	Diet (Hypocaloric), Exercise (Aerobic activities, Resistance training), Behavioral change
Food supplements	St. John's wort, Glucomannan, Chitosan, Chromium, Green tea, Ephedra
Drugs	Adipex-P®, Xenical®, Alli®, Qsymia®, Contrave®, Saxenda®, Wegovy®
Medical devices	Lap-Band® Adjustable Gastric Banding (LAGB®) System, Orbera® Intragastric Balloon System, Obalon® Balloon System, TransPyloric Shuttle® (TPS®), AspireAssist®, SmartByte Device, Plenity®
Gut microbiome modulation	Diet, Prebiotics, Probiotics, Synbiotics, Bariatric surgery, Fecal microbiota transplantation
Body contouring	Liposuction
Bariatric surgery	Sleeve gastrectomy, Roux-en-Y gastric bypass

Table 2. Anti-obesity tools approved and/or available in the USA (non-exhaustive list).

Any medical condition that can contribute to weight gain should be treated as appropriate. Subjects receiving medications known to induce weight gain should consider alternative treatment when possible.

Even a modest weight loss can decrease the risk of several comorbidities of obesity [6,29]. The ideal is a weight loss of at least 5 to 10% over 6 to 9 months followed by a long-lasting weight maintenance. Unfortunately, many subjects do not achieve long-lasting benefits of weight loss due to difficulty with compliance as well as body adaptation in response to weight loss.

Lifestyle

For a clinically meaningful weight loss, an intense lifestyle intervention that includes in-person individual or group sessions is recommended [6]. Diet is an important component in the management of obesity (Figure 6). Several hypocaloric diets have been proposed. They differ in the amount of calorie (e.g., low calorie or very-low calorie) and macronutrient composition (e.g.,

low or high carbohydrate, low or high fat, and high protein) [11]. Hypocaloric diets result in weight loss regardless of macronutrient composition. The extent of caloric restriction should be adjusted to the baseline caloric intake and the physical activity.

Figure 6: Appropriate diet is a key component of lifestyle. Copyright alexraths (Alexander Raths)/Depositphotos Inc.

Regular exercise including moderate intensity aerobic activities (3-5 weekly sessions with approximately 40 minutes per session) and resistance training is strongly recommended in the management of obesity (Figure 7).

Figure 7: Regular exercise is highly recommended in the management of obesity. Copyright MatoomMi (Janpen Chaiyadej)/ Depositphotos Inc.

Behavioral counseling is an essential component of lifestyle intervention and helps inducing a clinically meaningful weight loss [12].

Food Supplements

Food supplements are very appealing to people who desire losing weight. There are numerous products or combination of products available for weight loss that are reported to act through different mechanisms such as mood enhancement, increase in satiety, decrease in dietary fat absorption, modulation of carbohydrate metabolism, increase in fat oxidation/decrease in fat synthesis, and increase in energy expenditure. They include St. John's wort, glucomannan, chitosan, chromium, green tea, and ephedra (non-exhaustive list) [13]. However, there is no strong evidence for most of these preparations that they can cause clinically relevant weight loss without risk [14].

Drugs

Pharmacotherapy is considered for subjects with a BMI of at least 30 kg/m^2 or a BMI of at least 27 kg/m^2 in the presence of at least one comorbidity (e.g., type 2 diabetes). Several anti-obesity drugs with different mechanisms of action have been approved and are available worldwide [6,15,16]. Some anti-obesity drugs have been discontinued after several years of use due to adverse effects (e.g., Meridia and Belviq). Brown adipose tissue appears to be an attractive target for the treatment of obesity [1]. Below are the anti-obesity drugs approved and currently available in the USA (Table 3). Their use should always be in conjunction with lifestyle recommendations.

Drugs	Approval Years	Indications
Adipex-P®	1959	BMI ≥ 27 kg/m^2 (Short-term use)
Xenical®	1999	BMI ≥ 27 kg/m^2
Alli®	2007	BMI 27-< 30 kg/m^2 (Over-the-counter use)
Qsymia®	2012	BMI ≥ 27 kg/m^2
Contrave®	2014	BMI ≥ 27 kg/m^2
Saxenda®	2014	BMI ≥ 27 kg/m^2
Wegovy®	2021	BMI ≥ 27 kg/m^2

Table 3. Approved and available anti-obesity drugs in the USA ranked by the approval year.

Adipex-P® (Phentermine) is a noradrenergic agonist that causes a reduction in food intake. The adult dose is one capsule (37.5 mg) once a day (morning). Xenical® (Orlistat) is a gastric and pancreatic lipase inhibitor that causes a reduction in fat absorption. The adult dose is one capsule (120 mg) three times a day (morning, noon, evening). Alli® (Orlistat) is a gastric and pancreatic lipase inhibitor that causes a reduction in fat absorption. The adult dose is one capsule (60 mg) three times a day (morning, noon, evening). Qsymia® (Phentermine + Topiramate) is a combination of a noradrenergic agonist and a gamma-aminobutyric acid receptor agonist that causes a reduction in food intake. The adult maintenance dose is one capsule (Phentermine 15 mg/ Topiramate 92 mg) once a day (morning). Contrave® (Naltrexone + Bupropion) is a combination of an opioid receptor antagonist and an inhibitor of norepinephrine and dopamine transporters that causes a reduction in food intake. The adult maintenance dose is 2 tablets (Naltrexone 8 mg/Bupropion 90 mg) twice a day (morning, evening). Saxenda® (Liraglutide) is a glucagon-like peptide-1 receptor agonist that causes a reduction in food intake. The adult maintenance dose is 3 mg subcutaneously once a day. Wegovy® (Semaglutide) is a glucagon-like peptide-1 receptor agonist that causes a reduction in food intake. The adult maintenance dose is 2.4 mg subcutaneously once a week. The comparative efficacy of the above anti-obesity drugs is reported in Table 4.

Drugs	Treatment Duration	Total Body Weight Loss
Wegovy®	68 weeks	14.9%
Qsymia®	1 year	9.8%
Contrave®	56 weeks	8.1%
Saxenda®	56 weeks	7.4%
Xenical®	4 years	5.2%
Adipex-P®	3 months	3.0%

Table 4: Approved and available anti-obesity drugs in the USA ranked by the extent of total body weight loss in pivotal or other relevant studies.

The relevant or common adverse effects of the above anti-obesity drugs are reported in **Table 5**.

Drugs	Treatment Duration	Adverse Effects
Wegovy®	68 weeks	Abdominal pain, Constipation, Diarrhea, Dyspepsia, Nausea, Vomiting
Qsymia®	1 year	Constipation, Dizziness, Dry mouth, Dysgeusia, Insomnia, Paresthesia
Contrave®	56 weeks	Constipation, Dizziness, Dry mouth, Headache, Insomnia, Nausea, Vomiting
Saxenda®	56 weeks	Abdominal pain, Constipation, Diarrhea, Dyspepsia, Nausea, Vomiting
Xenical®	1 year	Fecal incontinence, Fecal urgency, Flatus, Oily spotting, Oily stool, Reduced absorption of fat-soluble vitamins
Adipex-P®	3 months	Anxiety, Increased blood pressure, Tremor

Table 5: Relevant or common adverse effects of the approved and available anti-obesity drugs in the USA in pivotal or other relevant studies in alphabetical order (non-exhaustive list).

The cost of the above anti-obesity drugs is reported in Table 6.

Drugs	Average Cost
Adipex-P®	$65/month
Xenical®	$730/month
Alli®	$60/month
Qsymia®	$200/month
Contrave®	$450/month
Saxenda®	$1,600/month
Wegovy®	$1,600/month

Table 6. Average cost (without insurance coverage) of the approved and available anti-obesity drugs in the USA.

In the USA, only a small number of subjects with obesity (around 2%) who are eligible for anti-obesity drugs receive drug therapy [15]. The reasons for this undertreatment rate are mainly related to the adverse effects and cost of drugs.

Medical Devices

Anti-obesity medical devices represent a heterogeneous family of devices offering an attractive approach in managing obesity [17]. They act mechanically without receptors, systemic absorption, or specific metabolism. Several anti-obesity medical devices have been approved/cleared in the USA, in Europe, and in other countries. Medical devices cause weight loss through different mechanisms (e.g., decrease in food intake and decrease in available/absorbed nutrients). Based on the expected weight loss, the Center for Devices and Radiological Health of the Food and Drug Administration in the USA categorizes anti-obesity medical devices as weight-loss devices or weight-management devices. The weight-loss devices include gastric band devices [e.g., Lap-Band® Adjustable Gastric Banding (LAGB®)], gastric space-occupying devices [e.g., Orbera® Intragastric Balloon System, Obalon® Balloon System, and TransPyloric Shuttle® (TPS®)], and gastric emptying devices (e.g., AspireAssist®). The weight-management devices include oral space-occupying devices (e.g., SmartByte Device) and gastric space-occupying devices (e.g., Plenity®). Below are the anti-obesity medical devices approved/cleared in the USA (Table 7). They should be used in conjunction with lifestyle recommendations. Some of the anti-obesity medical devices have limited availability.

Medical Devices	Approval Years	Indications
Lap-Band® Adjustable Gastric Banding (LAGB®) System	2001	BMI ≥ 35 kg/m^2 (Weight-loss device)
Orbera® Intragastric Balloon System	2015	BMI 30-40 kg/m^2 (Weight-loss device)
AspireAssist®	2016	BMI 35-55 kg/m^2 (Weight-loss device)
Obalon® Balloon System	2016	BMI 30-40 kg/m^2 (Weight-loss device)
SmartByte Device	2017	BMI 27-35 kg/m^2 (Weight-management device)
Plenity®	2019	BMI 25-40 kg/m^2 (Weight-management device)
TransPyloric Shuttle® (TPS®)	2019	BMI 30-40 kg/m^2 (Weight-loss device)

Table 7: Approved/cleared anti-obesity medical devices in the USA ranked by the approval year. Table modified from Heshmati HM (17).

Lap-Band® Adjustable Gastric Banding (LAGB®) System (BioEnterics Corporation) is an adjustable silicone band placed laparoscopically around the proximal stomach immediately below the gastro-esophageal junction and attached to a subcutaneous reservoir. The pressure imposed to the proximal stomach causes early satiety and a reduction in food intake.

Orbera® Intragastric Balloon System (Apollo Endosurgery, Inc.) is a balloon made of silicone placed endoscopically in the stomach (Figure 8). By occupying gastric volume, Orbera® Intragastric Balloon System causes early satiety and a reduction in food intake.

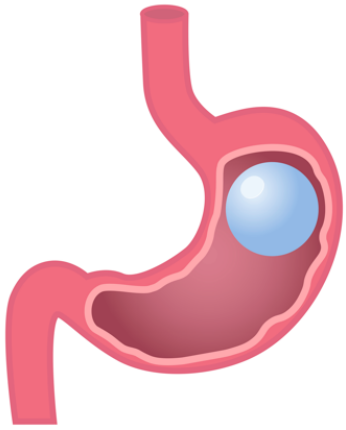

Figure 8: Intragastric balloon. Copyright fancy.tapis.gmail.com (Olga Nalynskaya)/Depositphotos Inc.

AspireAssist® (Aspire Bariatrics, Inc.) is a device attached to a percutaneous endoscopic gastrostomy tube implanted endoscopically. By allowing the removal of approximately 30% of ingested calories over 5-10 minutes, AspireAssist® causes a reduction in gastrointestinal nutrients absorption.

Obalon® Balloon System (Obalon Therapeutics, Inc.) is a swallowable balloon made of nylon and polyethylene contained within a gelatin capsule (attached to a thin inflation catheter) that is taken orally. By occupying gastric volume, Obalon® Balloon System causes early satiety and a reduction in food intake.

SmartByte Device (Scientific Intake) is an oral device occupying space on the upper palate. By creating limited bite size and slower eating, SmartByte Device causes a reduction in food intake.

Plenity® (Gelesis, Inc.) is a superabsorbent hydrogel (cellulose and citric acid, forming a three-dimensional matrix) administered orally in capsules with 500 mL of water (three capsules, 20-30 minutes before lunch and dinner). By creating a larger volume with higher elasticity in the stomach and intestine, Plenity® causes early satiety and a reduction in food intake.

TransPyloric Shuttle® (TPS®) (BAROnova, Inc.) is a device placed endoscopically in the stomach. By creating intermittent obstruction to gastric outflow that delays gastric emptying, TransPyloric Shuttle (TPS®) causes early satiety and a reduction in food intake.

The comparative effectiveness of the above anti-obesity medical devices is reported in Table 8.

Medical Devices	Treatment Duration	Total Body Weight Loss
Lap-Band® Adjustable Gastric Banding (LAGB®) System	36 months	18.0%
AspireAssist®	12 months	12.1%
Orbera® Intragastric Balloon System	6 months	10.2%
TransPyloric Shuttle® (TPS®)	12 months	9.5%
Obalon® Balloon System	6 months	6.6%
Plenity®	6 months	6.4%
SmartByte Device	4 months	1.7%

Table 8: Approved/cleared anti-obesity medical devices in the USA ranked by the extent of total body weight loss in pivotal studies. Table modified from Heshmati HM (17).

The relevant or common adverse effects of the above anti-obesity medical devices are reported in Table 9.

Medical Devices	Treatment Duration	Adverse Effects
Lap-Band® Adjustable Gastric Banding (LAGB®) System	36 months	Band erosion or migration, Proximal gastric enlargement, System leaks
AspireAssist®	12 months	Electrolyte abnormalities, Infection, Skin irritation
Orbera® Intragastric Balloon System	6 months	Balloon migration, Gastric perforation, Gastric ulcer, Intestinal obstruction
TransPyloric Shuttle® (TPS®)	12 months	Device impaction, Gastric ulcer
Obalon® Balloon System	6 months	Balloon migration, Gastric perforation, Gastric ulcer, Intestinal obstruction
Plenity®	6 months	Abdominal distension, Diarrhea, Infrequent bowel movements
SmartByte Device	4 months	Choking on food, Mouth soreness

Table 9: Relevant or common adverse effects of the approved/cleared anti-obesity medical devices in the USA in pivotal studies in alphabetical order (non-exhaustive list). Table modified from Heshmati HM (17).

The cost of the above anti-obesity medical devices is reported in Table 10.

Medical Devices	Average Cost
Lap-Band® Adjustable Gastric Banding (LAGB®) System	$15,000
Orbera® Intragastric Balloon System	$6,000
AspireAssist®	$10,000
Obalon® Balloon System	$8,000
SmartByte Device	$500
Plenity®	$100/month
TransPyloric Shuttle® (TPS®)	Information not available

Table 10: Average cost (without insurance coverage) of the approved/cleared anti-obesity medical devices in the USA. Table modified from Heshmati HM (17).

Gut Microbiome Modulation

Important changes (dysbiosis) affecting gut microbiome are associated with obesity (Figure 9). These changes include a decrease in gene richness, a higher abundance of Firmicutes phylum (with higher presence of *Lactobacillu*s genus), an increase in Firmicutes to Bacteroidetes phyla ratio, a lower abundance of Bacteroidetes phylum, and a lower abundance of Verrucomicrobia phylum (with lower presence of *Akkermansia* genus) [30].

Figure 9: Obesity is associated with important changes in gut microbiome (dysbiosis). Copyright ovocheva (Zhanna Kocherzhuk)/Depositphotos Inc.

Gut microbiome can be modulated to change the host metabolism and manage obesity. The tools include diet, prebiotics, probiotics, synbiotics, bariatric surgery, and gut microbiota transplantation. Diet (e.g., hypocaloric, low-fat, high-protein, and high-fiber diets) can increase the richness of gut microbiome and decrease the Firmicutes to Bacteroidetes phyla ratio and promote weight loss. Prebiotics (e.g., oligofructose-enriched inulin) and probiotics (e.g., fermented milk containing *Lactobacillus gasseri* species), by modulating gut microbiome, can manage weight gain and obesity. Bariatric surgery causes significant favorable changes in gut microbiome independently of body weight and further enhances weight loss. Clinical data on fecal microbiota transplantation in obesity are relatively limited but promising (Table 11) [18].

Tools	Description
Diet	Hypocaloric, Low fat, High protein, High fiber
Prebiotics	Inulin, Lactulose, Resistant starch
Probiotics	Milk, Yogurt, Cheese
Synbiotics	Combination of prebiotics and probiotics
Bariatric surgery	Roux-en-Y gastric bypass
Fecal microbiota transplantation	Addition of healthy stool

Table 11: Tools used for gut microbiome modulation in the management of obesity. Table modified from Heshmati HM (18).

The cost of gut microbiome modulation in the management of obesity is reported in Table 12.

Tools	Average Cost
Diet	Cost of food
Prebiotics	< $100/month
Probiotics	< $100/month
Synbiotics	< $100/month
Bariatric surgery (Roux-en-Y gastric bypass)	$23,000
Fecal microbiota transplantation	$1,800 + Cost of administration/dose

Table 12: Average cost (without insurance coverage) of tools used for gut microbiome modulation in the management of obesity in the USA. Table modified from Heshmati HM (18).

Body Contouring

The remodeling of the body contour is achievable through several invasive or noninvasive methods. Liposuction is the most popular cosmetic procedure in the world and is considered safe for remodeling the body contour [19-22]. It is mainly used for the correction of deep and superficial fat accumulations. Small incisions are performed in different places depending on the area that needs treatment. A cannula is inserted, and the adipose tissue is broken loose from the fibrous stroma with multiple crisscross movements and removed (Figure 10). When properly performed, complications of liposuction are rare. To improve aesthetic results, excision surgery may be necessary for removing the excess skin.

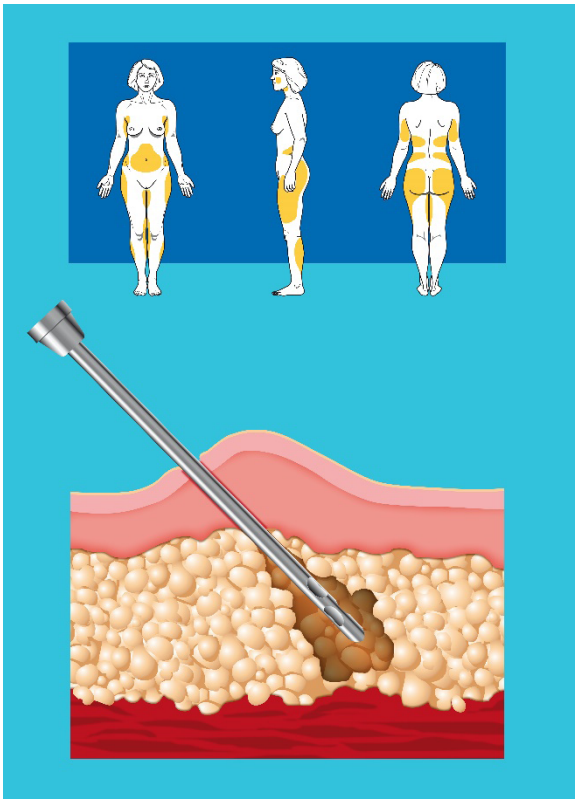

Figure 10: Liposuction remodels the body contour by correcting deep and superficial fat accumulations. Copyright alexonline (ALESSANDRO INNAMORATI)/Depositphotos Inc.

The liposuction technique developed rapidly since the 1970s. After the traditional liposuction technique (suction-assisted liposuction), several adjunct technologies have been developed using ultrasound, power, laser, water, and radiofrequency [19]. Cryolipolysis is also a promising safe and efficient noninvasive technology for body contouring [31]. All these methods differ from each other by their mechanism of action, their response rate, their side effects, and the number of treatments required.

Bariatric Surgery

Bariatric surgery is an established and effective treatment for morbid obesity. It is indicated in subjects with a BMI of at least 40 kg/m^2 or a BMI of at least 35 kg/m^2 in the presence of at least one comorbidity (e.g., type 2 diabetes). Bariatric surgery procedure can be restrictive (e.g., sleeve gastrectomy), malabsorptive (e.g., intestinal bypass), or mixed (e.g., Roux-en-Y gastric bypass) [6,23,24]. The most common bariatric surgery procedures in the USA are sleeve gastrectomy and Roux-en-Y gastric bypass. With sleeve gastrectomy, a staple line is placed along the greater curvature of the stomach and there is a removal of approximately 80% of the lateral aspect of the stomach in a vertical fashion. With Roux-en-Y gastric bypass, a small stomach pouch is created in the upper stomach, the jejunum is divided, and the middle part of it (the Roux limb) is connected to the stomach pouch.

Bariatric surgery induces significant weight loss (at least 20%) and dramatically reduces the comorbidities of obesity (e.g., prediabetes, type 2 diabetes, dyslipidemia, and hypertension) while having a low mortality rate (less than 1%) [23,24]. Roux-en-Y gastric bypass is associated with the largest sustained weight loss. Also, through multiple mechanisms (e.g., reduced caloric intake, reduced gastric emptying, alterations in gastric acid production and bile acids, modifications of gut hormones, and malabsorption), bariatric surgery produces long-term alterations of gut microbiome (e.g., gene richness and composition) independently of body weight (Figure 11) [32]. These changes counteract those observed in obesity and can further affect body weight regulation by enhancing weight loss.

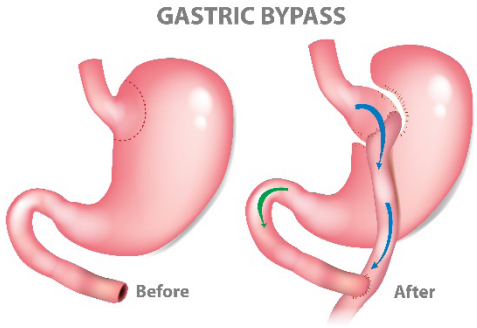

Figure 11: Roux-en-Y gastric bypass causes significant changes in the gut microbiome (e.g., gene richness and composition), further enhancing weight loss. Copyright Sakurra (Viktoriia Kasianiuk)/ Depositphotos Inc.

The relevant or common adverse effects of body contouring and bariatric surgery are reported in Table 13.

Tools	Adverse Effects
Body contouring (Liposuction)	Contour irregularity, Hematoma, Infection, Seroma
Bariatric surgery	Hemorrhage, Infection, Leak, Mineral and vitamin deficiencies, Ulceration

Table 13: Relevant or common adverse effects of body contouring and bariatric surgery in alphabetical order (non-exhaustive list).

The costs of body contouring and bariatric surgery are reported in Table 14.

Tools	Average Cost
Body contouring (Liposuction)	$3,650/area
Bariatric surgery (Sleeve gastrectomy)	$9,350
Bariatric surgery (Roux-en-Y gastric bypass)	$23,000

Table 14: Average cost (without insurance coverage) of body contouring and bariatric surgery in the USA.

In the USA, less than 1% of subjects with obesity who are eligible for bariatric surgery benefits from it. The reasons for this undertreatment rate are mainly related to adverse effects and cost of bariatric surgery.

Special Populations

Special populations impacted by excess adiposity include children and adolescents, elderly subjects, pregnant women, and subjects with type 2 diabetes (non-exhaustive list).

Children and Adolescents

Pediatric obesity is a serious public health issue that will challenge health providers for many years to come [33-36]. The worldwide number of children and adolescents with obesity is approximately 100 million (Figure 12). The prevalence of pediatric obesity in the USA is around 19%. The risk of adult obesity is at least 2 times greater for children with obesity than for children without obesity. The associated comorbidities in youth with obesity (e.g., prediabetes, type 2 diabetes, dyslipidemia, and hypertension) can impact the adulthood health and longevity.

Figure 12: Pediatric obesity is becoming a major health challenge worldwide. Copyright agnieszka (Agnieszka Terenowska)/ Depositphotos Inc.

In addition to preventive measures, pediatric obesity can be managed with multidisciplinary approaches including lifestyle (diet, exercise, and behavioral change), drugs (e.g., Xenical®, Adipex-P®, and Saxenda®), and bariatric surgery [33-36]. However, lifestyle interventions should be the first-line therapy in the management of pediatric obesity.

Elderly Subjects

Over the last several decades, there has been a dramatic expansion of the elderly population. By the year 2030, at least 20% of the population of the USA will be aged 65 years or older. Geriatric obesity is a growing global health concern. In the USA, the prevalence of geriatric obesity using BMI criteria parallels the prevalence of non-geriatric obesity (> 33%) [10]. Interestingly, centenarians have a lower prevalence of overweight and obesity [37]. Geriatric obesity can cause impaired physical function, decreased quality of life, several comorbidities, institutionalization, and ultimately death [10,38].

Weight loss intervention in older subjects is a controversial topic [10,38]. Several studies have shown that increased adiposity may have a protective effect in older adults. Due to the high prevalence of sarcopenia in old subjects, BMI is not a reliable marker for the management of obesity as it may not accurately reflect the adipose tissue mass. In several cases, because of the potential risk for aggravation of sarcopenia and osteopenia, weight maintenance rather that weight loss may be the most prudent approach (Figure 13).

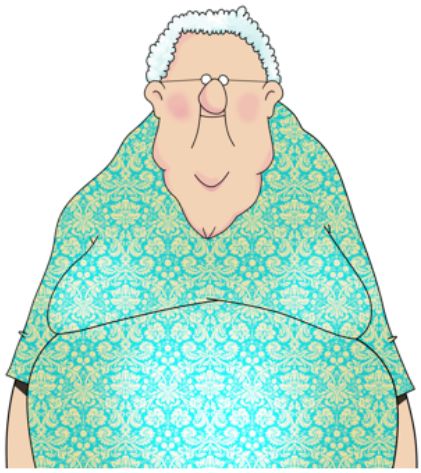

Figure 13: The management of obesity in the elderly population is a new medical challenge. Copyright ponytail1414 (Leslie Murray)/ Depositphotos Inc.

Pregnant Women

Obesity during pregnancy is a growing health problem worldwide. In Western countries, the prevalence of obesity in pregnant women is around 30% (Figure 14). Obesity can increase maternal, fetal, and neonatal risks (e.g., gestational diabetes,

gestational hypertension, preeclampsia, congenital defects, preterm birth, and stillbirth) [39-41]. Chronic fetal hypoxia is a potential contributing factor [42]. Maternal obesity can also cause major cardiovascular events later in life [39]. Epigenetic alterations may be responsible for this outcome [41].

Figure 14: Approximately 30% of pregnant women in Western countries have obesity. Copyright Morphart (Patrick Guénette)/ Depositphotos Inc.

Pregnancy in women with obesity should be considered and managed as a high-risk condition. Weight loss before pregnancy is the most effective way to reduce maternal and fetal risks.

Subjects with Type 2 Diabetes

Type 2 diabetes is a global pandemic [43]. In the USA, the numbers of adult subjects with type 2 diabetes is around 35 million. Type 2 diabetes is closely related to overweight and obesity. Around 30% of subjects with obesity have type 2 diabetes. Among subjects with type 2 diabetes, at least 85% have overweight or obesity.

Weight loss is an important objective in the treatment of most subjects with type 2 diabetes. However, weight loss in these individuals has usually been a challenge [44]. Fasting plasma glucose and several antidiabetic drugs can impact body weight and the efficacy of weight-loss programs (Figure 15). If subjects are on hypocaloric diet alone, as glycemic control improves, urinary glucose decreases or disappears leading to a reduction of weight loss or a weight gain. The weight loss in these subjects usually reaches a plateau after 6 months [44]. Antidiabetic drugs can either promote weight loss (e.g., biguanides and glucagon-like peptide-1 agonists), be weight neutral (e.g., alpha-glucosidase inhibitors and dipeptidyl peptidase-4 inhibitors), or cause weight gain (e.g., insulin and sulfonylureas). When combined with lifestyle changes in a weight-loss program, antidiabetic drugs can either potentiate or antagonize weight loss. The weight loss and weight gain caused by these drugs usually occur within the first year of treatment. The extent of weight change can be up to approximately 4 to 5 kg for either weight loss or weight gain [45]. Treatment decision for the use of antidiabetic drugs should give priority to weight-friendly strategies.

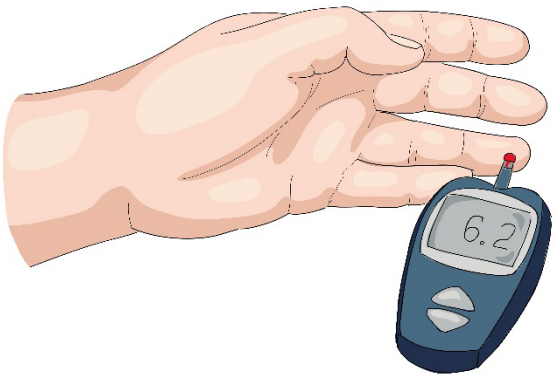

Figure 15: The efficacy of weight-loss programs can be impacted by fasting plasma glucose and antidiabetic drugs. Copyright grib_ nick (Andrii Kovalenko)/Depositphotos Inc.

Deficient Adiposity

Lipodystrophies are examples of deficient adiposity. They are heterogeneous disorders characterized by selective loss of body fat and predisposition to insulin resistance. They can be genetic (e.g., Berardinelli-Seip syndrome and mandibuloacral dysplasia-associated lipodystrophy) or acquired (e.g., Lawrence syndrome and Barraquer-Simons syndrome), partial or generalized [46,47].

Conclusion

Excess adiposity is the expansion of adipose tissue leading to overweight/obesity. Obesity is a major health problem worldwide causing multiple comorbidities, high mortality, and high cost for the society. Management of excess adiposity requires multidisciplinary approaches including lifestyle (e.g., diet, exercise, and behavioral change), food supplements, drugs, medical devices, gut microbiome modulation, body contouring, and bariatric surgery. Long-term weight maintenance is a challenging goal for most patients and physicians.

References

1. Saely CH, Geiger K, Drexel H (2012) Brown versus white adipose tissue: A mini-review. Gerontology 58: 15-23.
2. Yu P, Yuan R, Yang X, Qi Z (2019) Adipose tissue, aging, and metabolism. Curr Opin Endocr Metab Res 5: 11-20.
3. Nauli AM, Matin S (2019) Why do men accumulate abdominal visceral fat? Front Physiol 10: 1486.
4. Frasca D, Blomberg BB (2020) Adipose tissue, immune aging, and cellular senescence. Semin Immunopathol 42: 573-587.
5. Chait A, den Hartigh LJ (2020) Adipose tissue distribution, inflammation and its metabolic consequences, including diabetes and cardiovascular disease. Front Cardiovasc Med 7: 22.
6. Gadde KM, Martin CK, Berthoud HR, Heymsfield SB (2018) Obesity. Pathophysiology and management. J Am Coll Cardiol 71: 69-84.
7. Di Angelantonio E, Bhupathiraju SN, Wormser D, Gao P, Kaptoge S, et al. (2016) Body-mass index and all-cause mortality: Individual-participant-data meta-analysis of 239 prospective studies in four continents. Lancet 388: 776-786.
8. Afshin A, Forouzanfar MH, Reitsma MB, Sur P, Estep K, et al. (2017) Health effects of overweight and obesity in 195 countries over 25 years. N Engl J Med 377: 13-27.
9. Shephard RJ (2019) On determining how much obesity is costing society. HFJC 12: 80-116.
10. Malenfant JH, Batsis JA (2019) Obesity in the geriatric population-A global health perspective. JoGHR 3: e2019045.
11. Freedman MR, King J, Kennedy E (2001) Popular diets: A scientific review. Obes Res 9 (Suppl 1): 1S-40S.
12. Wadden TA, Butryn ML, Hong PS, Tsai AG (2014) Behavioral treatment of obesity in patients encountered in primary care settings. A systematic review. JAMA 312: 1779-1791.
13. Saper RB, Eisenberg DM, Phillips RS (2004) Common dietary supplements for weight loss. Am Fam Physician 70: 1731-1738.
14. Onakpoya IJ, Wider B, Pittler MH, Ernst E (2011) Food supplements for body weight reduction: A systematic review of systematic reviews. Obesity (Silver Spring) 19: 239-244.
15. Saxon DR, Iwamoto SJ, Mettenbrink CJ, McCormick E, Arterburn D, et al. (2019) Antiobesity medication use in 2.2 million adults across eight large health care organizations: 2009-2015. Obesity (Silver Spring) 27: 1975-1981.
16. Wilding JPH, Batterham RL, Calanna S, Davies M, Van Gaal LF, et al. (2021) Once-weekly Semaglutide in adults with overweight or obesity. N Engl J Med 384: 989-1002.
17. Heshmati HM (2020) Anti-obesity medical devices. In: Weight Management. Himmerich H (ed), IntechOpen, London, p. 239-253.
18. Heshmati HM (2020) Gut microbiome in obesity management. In: Weight Management. Himmerich H (ed), IntechOpen, London, p. 255-268.
19. Shridharani SM, Broyles JM, Matarasso A (2014) Liposuction devices: Technology update. Med Devices: Evid Res 7: 241-251.
20. Kaoutzanis C, Gupta V, Winocour J, Layliev J, Ramirez R, et al. (2017) Cosmetic liposuction: Preoperative risk factors, major complication rates, and safety of combined procedures. Aesthet Surg J 37: 680-694.
21. Bellini E, Grieco MP, Raposio E (2017) A journey through liposuction and liposculture: Review. Ann Med Surg 24: 53-60.
22. Wu S, Coombs DM, Gurunian R (2020) Liposuction: Concepts, safety, and techniques in body-contouring surgery. Cleve Clin J Med 87: 367-375.
23. Pories WJ (2008) Bariatric surgery: Risks and rewards. J Clin Endocrinol Metab 93: S89-S96.
24. Radvinsky D, Iskandar M, Ferzli G (2017) Bariatric surgery today: The good, the bad, and the ugly. Ann Laparosc Endosc Surg 2: 52.
25. Mancuso P, Bouchard B (2019) The impact of aging on adipose function and adipokine synthesis. Front Endocrinol 10: 137.
26. Hunter GR, Gower BA, Kane BL (2010) Age related shift in visceral fat. Int J Body Compos Res 8: 103-108.
27. Heshmati HM (2022) Endocrine-disrupting chemicals and related medical disorders. Rep Glob Health Res 5: 140.
28. Elffers TW, de Mutsert R, Lamb HJ, de Roos A, Willems van Dijk K, et al. (2017) Body fat distribution, in particular visceral fat, is associated with cardiometabolic risk factors in obese women. PLoS One 12: e0185403.
29. Goldstein DJ (1992) Beneficial health effects of modest weight loss. Int J Obes (Lond) 16: 397-415.
30. Pinart M, Dötsch A, Schlicht K, Laudes M, Bouwman J, et al. (2022) Gut microbiome composition in obese and non-obese persons: A systematic review and meta-analysis. Nutrients 14: 12.
31. Krueger N, Mai SV, Luebberding S, Sadick NS (2014) Cryolipolysis for noninvasive body contouring: Clinical efficacy and patient satisfaction. Clin Cosmet Investig Dermatology 7: 201-205.
32. Debédat J, Clément K, Aron-Wisnewsky J (2019) Gut microbiota dysbiosis in human obesity: Impact of bariatric surgery. Curr Obes Rep 8: 229-242.
33. Cuda SE, Censani M (2019) Pediatric obesity algorithm: A practical approach to obesity diagnosis and management. Front Pediatr 6: 431.
34. Ameer B, Weintraub MA (2018) Pediatric obesity: Influence on drug dosing and therapeutics. J Clin Pharmacol 58: S94-S107.
35. Srivastava G, Fox CK, Kelly AS, Jastreboff AM, Browne AF, et al. (2019) Clinical considerations regarding the use of obesity pharmacotherapy in adolescents with obesity. Obesity (Silver Spring) 27: 190-204.
36. Kelly AS, Auerbach P, Barrientos-Perez M, Gies I, Hale PM, et al. (2020) A randomized, controlled trial of Liraglutide for adolescents with obesity. N Engl J Med 382: 2117-2128.
37. Pereira da Silva A, Matos A, Valente A, Gil Â, Alonso I, et al. (2016) Body composition assessment and nutritional status evaluation in men and women Portuguese centenarians. J Nutr Health Aging 20: 256-266.
38. DeCaria JE, Sharp C, Petrella RJ (2012) Scoping review report: Obesity in older adults. Int J Obes (Lond) 36: 1141-1150.

39. Lee KK, Raja EA, Lee AJ, Bhattacharya S, Bhattacharya S, et al. (2015) Maternal obesity during pregnancy associates with premature mortality and major cardiovascular events in later life. Hypertension 66: 938-944.

40. Melchor I, Burgos J, del Campo A, Aiartzaguena A, Gutiérrez J, et al. (2019) Effect of maternal obesity on pregnancy outcomes in women delivering singleton babies: A historical cohort study. J Perinat Med 47: 625-630.

41. Reichetzeder C (2021) Overweight and obesity in pregnancy: Their impact on epigenetics. Eur J Clin Nutr 75: 1710-1722.

42. Åmark H, Sirotkina M, Westgren M, Papadogiannakis N, Persson M (2020) Is obesity in pregnancy associated with signs of chronic fetal hypoxia? Acta Obstet Gynecol Scand 99: 1649-1656.

43. Zhou B, Lu Y, Hajifathalian K, Bentham J, Di Cesare M, et al. (2016) Worldwide trends in diabetes since 1980: A pooled analysis of 751 population-based studies with 4.4 million participants. Lancet 387: 1513-1530.

44. Pi-Sunyer FX (2005) Weight loss in type 2 diabetic patients. Diabetes Care 28: 1526-1527.

45. Hollander P (2007) Anti-diabetes and anti-obesity medications: Effects on weight in people with diabetes. Diabetes Spectr 20: 159-165.

46. Garg A (2011) Lipodystrophies: Genetic and acquired body fat disorders. J Clin Endocrinol Metab 96: 3313-3325.

47. Cortés VA, Fernández-Galilea M (2015) Lipodystrophies: Adipose tissue disorders with severe metabolic implications. J Physiol Biochem 71: 471-478.