Obesity from gynecological perspective

September.16th 2022

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Obesity is recognised as a disease and health issue

WOF

"The World Obesity Federation takes the position that obesity is a chronic, relapsing, progressive disease process and emphasizes the need for immediate action for prevention and control of this global epidemic"[1]

World Obesity Federation

OC

"Obesity is characterized by excess body fat that can threaten or affect your health. Many organizations including Obesity Canada, now consider obesity to be a chronic disease."[4]

Obesity Canada

AMA

"American Medical Association recognizes obesity and overweight as a chronic medical condition (de facto disease state) and urgent public health problem…and work towards the recognition of obesity intervention as an essential medical service…"[2]

American Medical Association

EASO

"A progressive disease, impacting severely on individuals and society alike, it is widely acknowledged that obesity is the gateway to many other disease areas…"[5]

European Association for the Study of Obesity

FDA

"Obesity is a chronic relapsing health risk defined by excess body fat"[3]

The US Food and Drug Administration

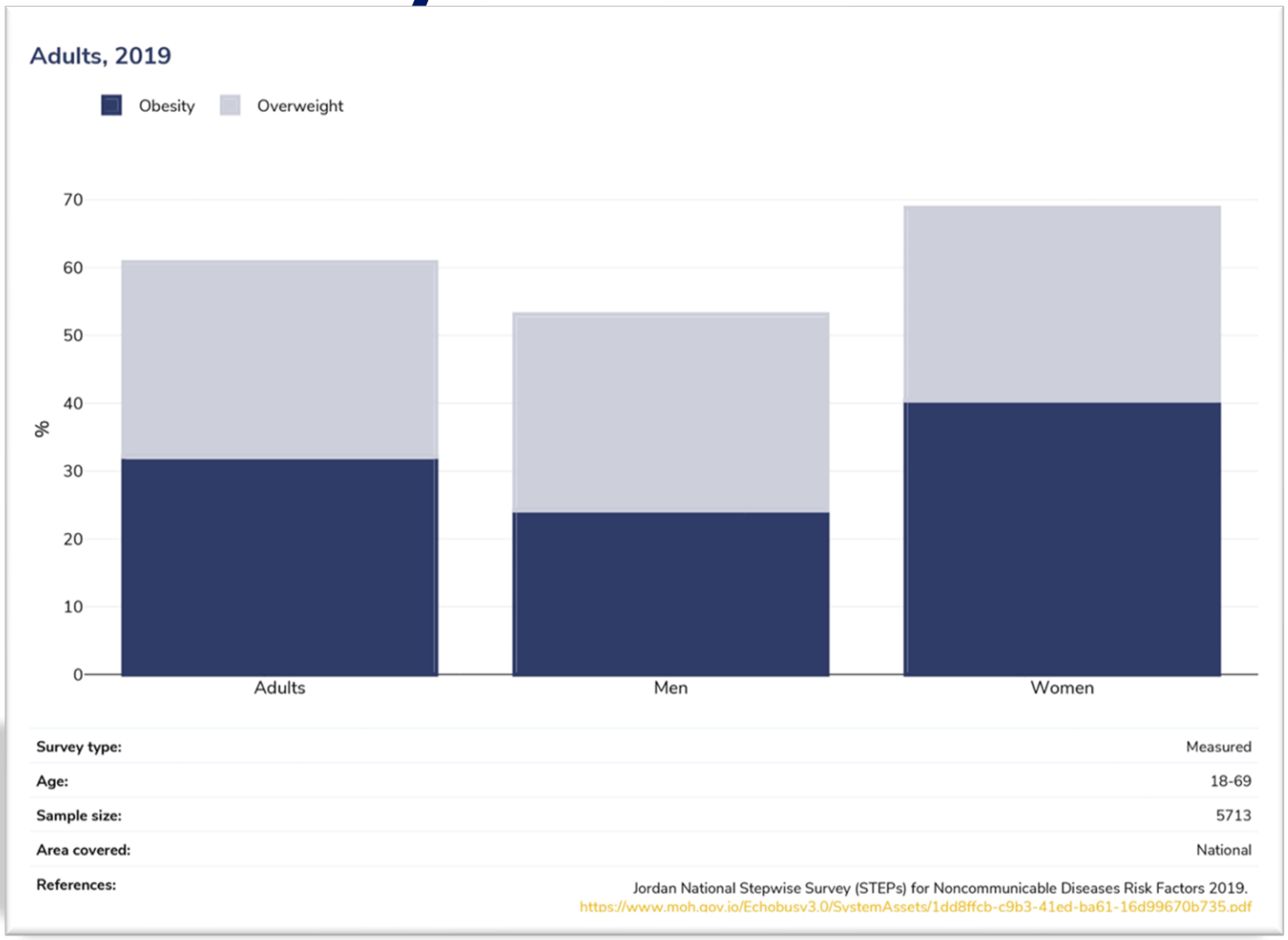
EMA

"Obesity is recognised as a chronic clinical condition and is considered to be the result of interactions of genetic, metabolic, environmental and behavioural factors, and is associated with increases in both morbidity and mortality"[6]

European Medicines Agency

Bray *et al*. *Obes Rev* 2017;18:715–23; 2. AMA resolutions. June 2012. Available here; 3. Food and Drug Administration. Guidance for Industry Developing Products for Weight Management 2007 Available here; 4. Obesity Canada. Available here; 5. EASO: 2015 Milan Declaration: A Call to Action on Obesity. Available here; 6. EMA Draft Guideline on clinical evaluation of medicinal products used in weight control EMA/CHMP/311805/2014. Available here.

Prevalence of obesity in Jordan

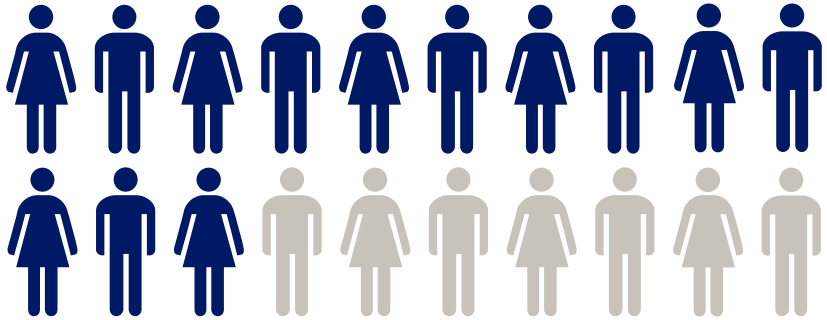


https://www.moh.gov.jo/Echobusv3.0/SystemAssets/1dd8ffcb-c9b3-41ed-ba61-16d99670b735.pdf

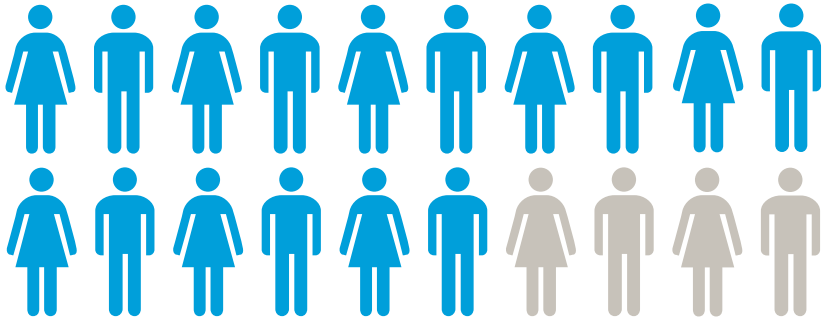
Obesity disease recognition

Results from the US ACTION study

65% of PwO recognise obesity as a disease



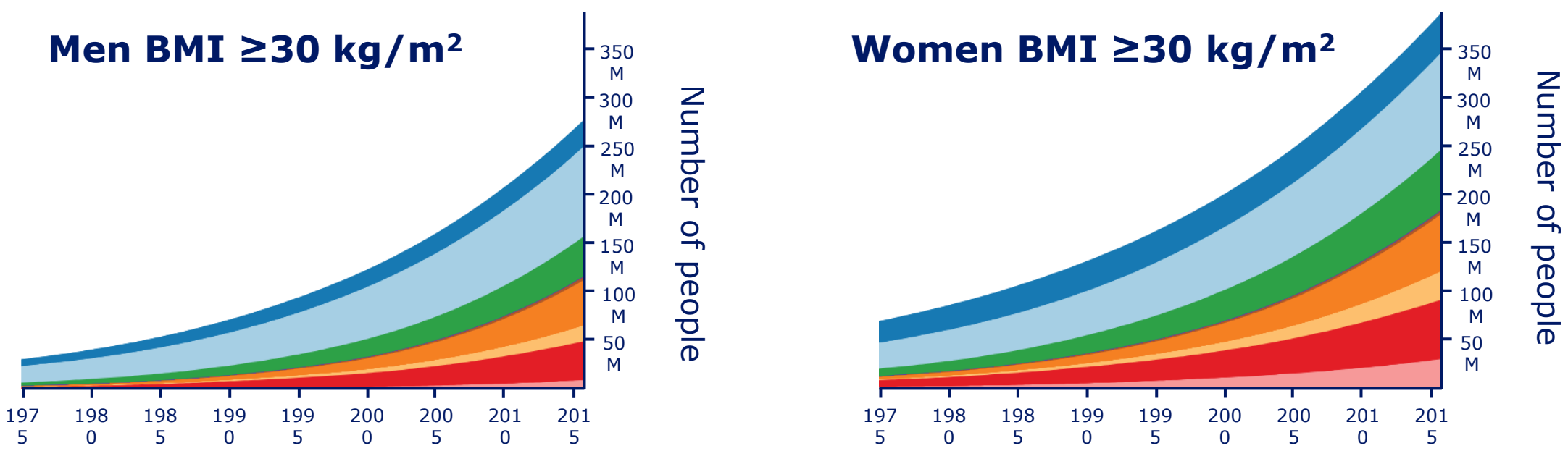
80% of HCPs recognise obesity as a disease



HCP, healthcare provider; PwO, people with obesity

Kaplan *et al. Obesity (Silver Spring).* 2018;26:61-69

Obesity rates worldwide are increasing



- WHO estimates that more than 1 billion people are overweight, with 300 million meeting the criteria for obesity.
- 26% of nonpregnant women ages 20-39 are overweight and 29% are obese.

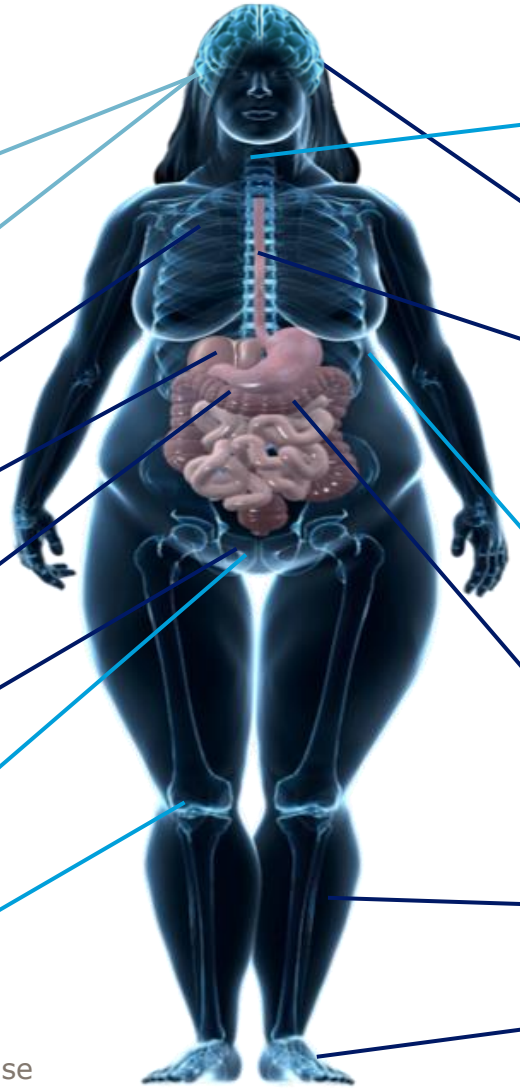
M, million

Adapted from NCD Risk Factor Collaboration (NCD-RisC). *Lancet* 2017:390;2627–42

Obesity is associated with multiple comorbidities

Metabolic, mechanical and mental

- Metabolic
- Mechanical
- Mental
- Cancers*
- Physical functioning



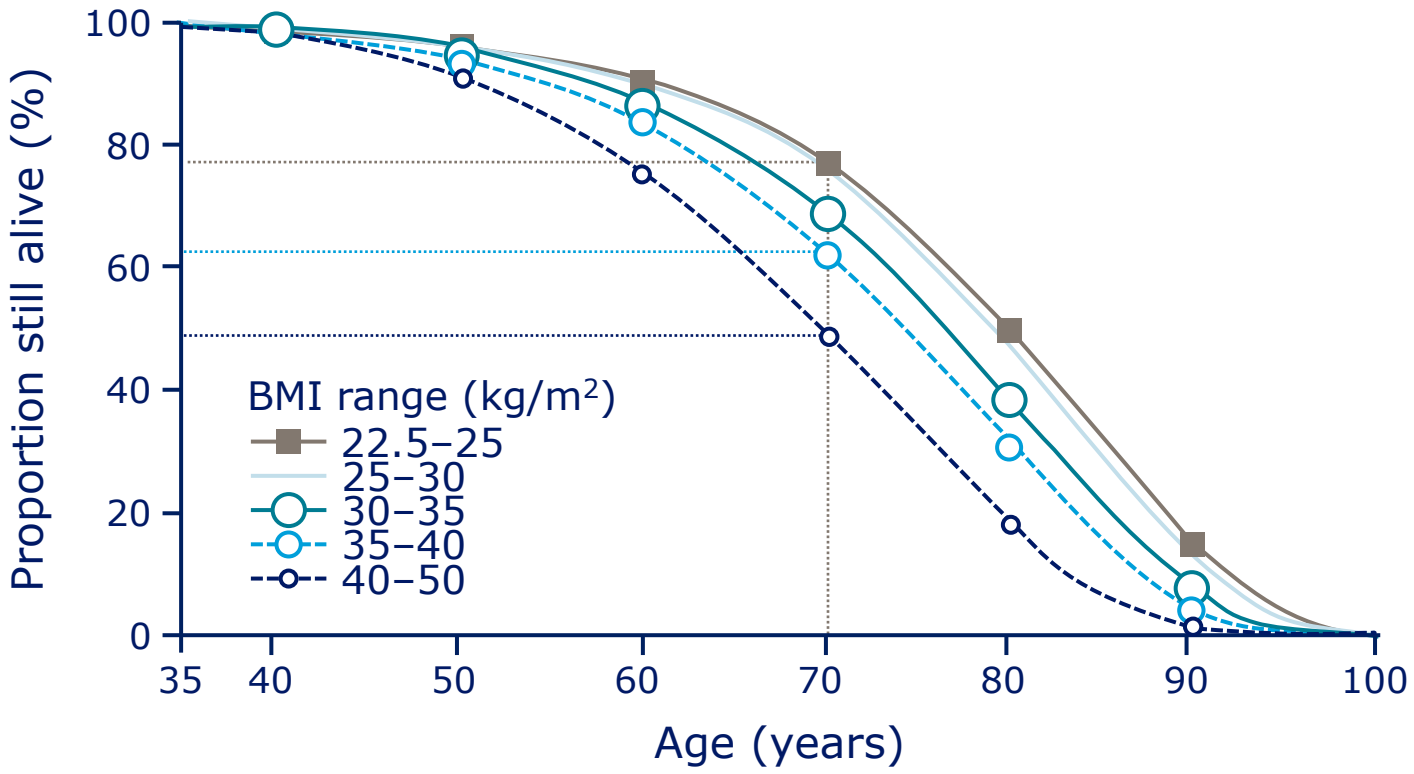
- Depression
- Anxiety
- Asthma
- NAFLD
- Gallstones
- Infertility
- Incontinence
- Arthrosis

- Sleep apnoea
- CVD and risk factors
  - Stroke
  - Dyslipidaemia
  - Hypertension
  - Coronary artery disease
  - Congestive heart failure
  - Pulmonary embolism
- Chronic back pain
- Type 2 diabetes
  Prediabetes
- Thrombosis
- Gout

CVD, cardiovascular disease; NAFLD, non-alcoholic fatty liver disease
*Including breast, colorectal, endometrial, esophageal, kidney, ovarian, pancreatic and prostate

Adapted from Sharma AM. *Obes Rev*. 2010;11:808-9; Guh *et al. BMC Public Health* 2009;9:88; Luppino *et al. Arch Gen Psychiatry* 2010;67:220–9; Simon *et al. Arch Gen Psychiatry* 2006;63:824–30; Church *et al. Gastroenterology* 2006;130:2023–30; Li *et al. Prev Med* 2010;51:18–23; Hosler. *Prev Chronic Dis* 2009;6:A48

Life expectancy decreases as BMI increases



Normal BMI =
almost 80% chance
of reaching age 70

BMI 35–40 =
~60% chance of reaching age 70

BMI 40–50 =
~50% chance of reaching age 70

Data are based on male subjects; n=541,452

Prospective Studies Collaboration. *Lancet* 2009;373:1083–96

Obesity and Women Health

Effects on fertility and fecundity

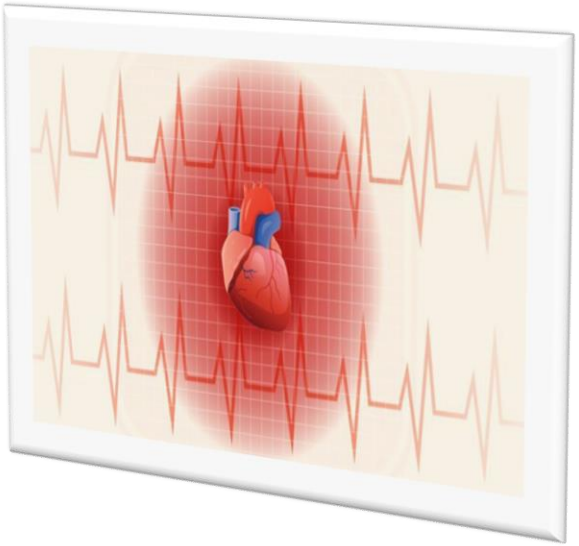
Women obesity and related co-morbidities

CAD

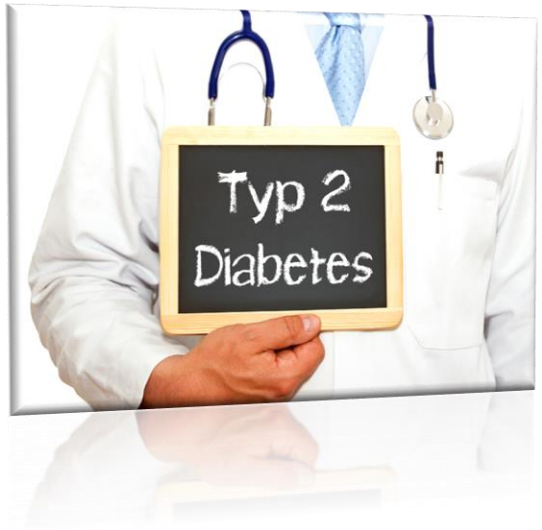
Obesity is an independent risk factor for the development of (CAD) in women and is a modifiable risk factor for prevention of CAD.

The mechanism of action is likely the relationship between obesity and insulin resistance.

A meta-analysis that included data on more than 22,000 patients (72% women) looking at the relationship between bariatric surgery and cardiovascular risk factors found that hyperlipidemia improved in 70% of patients after surgery and hypertension was resolved in 62% and improved in 78%



Women obesity and related co-morbidities



NIDDM

The risk of diabetes mellitus (DM) increases with the degree and duration overweight or obese.

Increased visceral fat enhances the degree of insulin resistance associated with obesity.

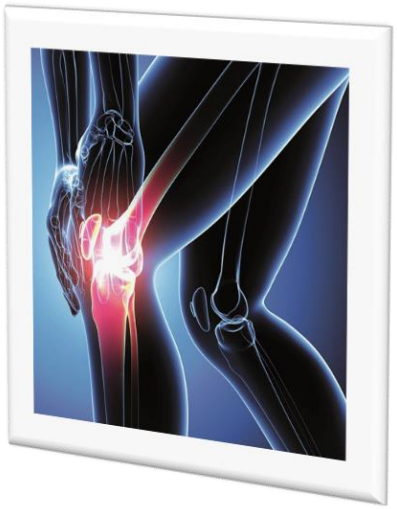
A systematic review that included more than 135,000 patients (80% women) found that bariatric surgery resulted in complete resolution of diabetes in 78% of patients and improvement in diabetic control in more than 86% of patients.

Women obesity and related co-morbidities

Musculoskeletal Pain

In the United States, the Center for Disease Control and Prevention statistics show that more than 31% of obese adults reported arthritis compared with only 16% of nonobese adults.

Obesity has been implicated in the development or progression of low back pain and knee osteoarthritis (OA) in women.



Women obesity and related co-morbidities

Table 3. Effects of Obesity on Knee Osteoarthritis

Authors	Assessment of Obesity	Results	Effect* (OR [RR])
Abbate et al (30)	BMI: heaviest quartile vs lowest quartile	Increased diagnosis of knee OA	5.27 (3.05–9.13)
	Weight: heaviest quartile vs lowest quartile	Increased diagnosis of knee OA	5.28 (3.05–9.16)
Grotle et al (31)	BMI >30	Increased diagnosis of new knee OA within 10 years	2.81 (1.32–5.96)
Holmberg et al (32)	BMI increase from 23 to 25	Increased radiograph diagnosis of knee OA	1.6 (0.9–3.1)
Liu et al (33)	BMI >30 vs BMI <22.5	Increased rates of knee replacement	10.51 (7.85–14.08)
Patterson et al (12)	BMI >35	Increased rates of knee replacement	11.7

*All odds ratio (OR) and relative risk (RR) are compared to women with body mass index (BMI) <25, unless otherwise noted.
OA, osteoarthritis.

knee OA

The factors underlying the association of obesity with knee OA have not been entirely elucidated.

Obesity leads to an excess load on the joint, increased cartilage turnover, increased collagen type 2 degradation products, and increased risk of degenerative meniscal lesions.

Although all of these have been theorized to lead to knee OA no causal relationships have been demonstrated to date

Dietary weight loss in combination with exercise effectively led to significant improvements in pain and physical function in women with knee OA over 18 months

Women obesity and related co-morbidities

low back pain

Obesity increases the risk of low back pain onset for women within 10 years .

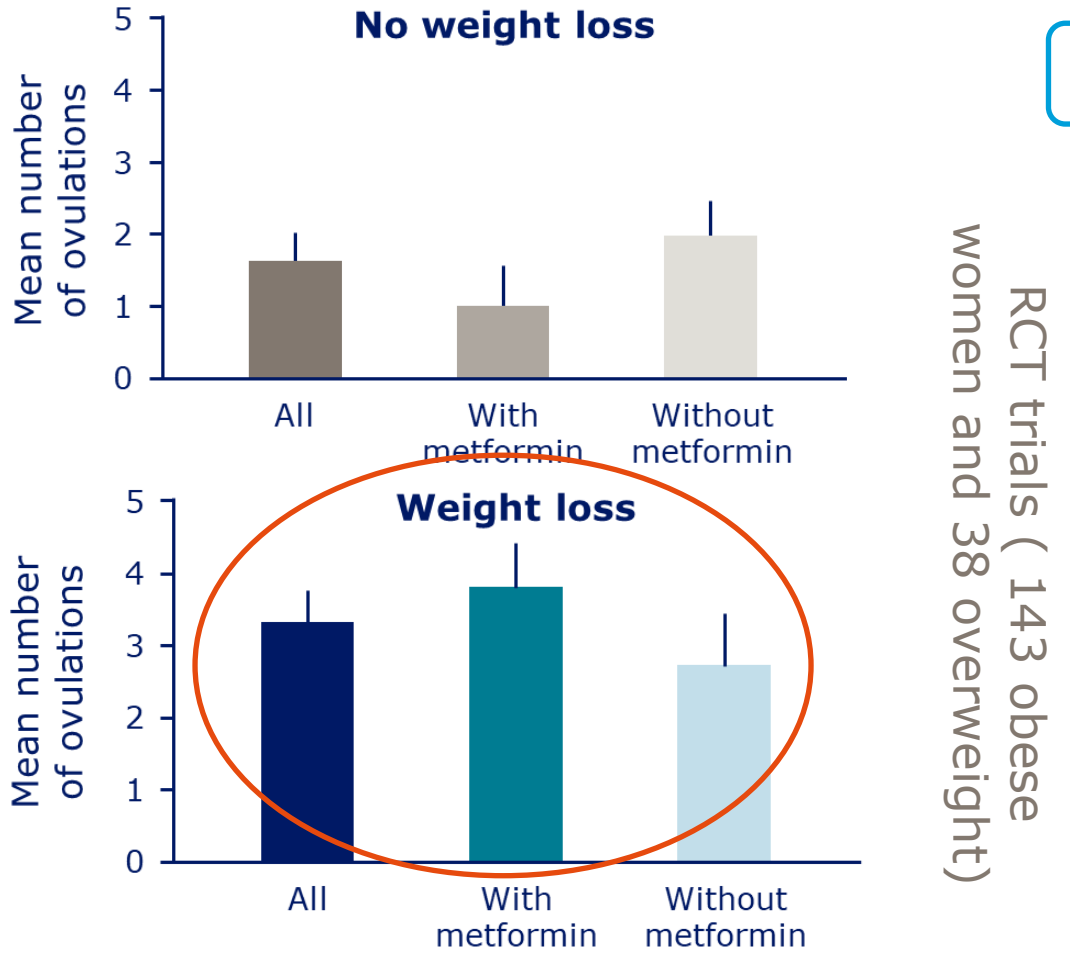
The increased burden of obesity is more obvious as women age, with significantly more obese women over the age of 40 reporting low back pain and lumbosacral radicular symptoms.

Symptoms increase further in obese women over the age of 54.

This data supports the theory that obesity over time contributes to low back pain and that weight loss may help prevent the onset of low back pain in obese women.

There is no evidence to support the recommendation of weight loss to treat low back pain once the pain is present

Women obesity and related co-morbidities



RCT trials (143 obese women and 38 overweight)

Weight loss improves fertility in women with PCOS

PCOS

The impact of obesity and Polycystic Ovary Syndrome (PCOS) on reproductive function can be attributed to multiple endocrine mechanisms.

Abdominal obesity is associated with an increase in circulating insulin levels.

This results in increased functional androgen levels (caused by suppression of sex hormone–binding globulin synthesis and increased ovarian androgen production).

Hyperandrogenism and menstrual cycle abnormalities are clinically manifested in part by anovulatory cycles and subfertility.

Although obesity may amplify the effects of PCOS, it is not a diagnostic criteria for PCOS.

1. Tang *et al. Hum Reprod* 2006;21:80–9; 2. Hoeger *et al. Fertil Steril* 2004;82:421–9

Women obesity and related co-morbidities

Depression

Some studies found an association between obesity and higher rates of depression in women but not in men

Others reported inverse associations between obesity and depression in both women and men

Although many social, psychological, and cultural factors likely contribute to the development of depression in obese women.

One explanation argues that the stigma toward obese individuals leads to low self-esteem and ultimately depression.

Obesity and Cancer in Women

- Obesity is a risk factor for developing women cancers.
- No current consensus regarding appropriate chemotherapy dosing for the obese patients.
- High endogenous estrogen contribute to higher risk of several types of cancer.

Endometrial Cancer

Endometrial carcinoma is strongly related to obesity.

In premenopausal women, anovulation or oligo-ovulation results in an endometrium proliferation and the potential for neoplastic changes.

a 2- to 5-fold increased risk of developing endometrial carcinoma in premenopausal and postmenopausal women.

Obesity has been associated with at least 40% of the incidence of endometrial cancer

Ovarian Cancer

increased risk of ovarian cancer in obese women focuses on the hormonal impact of obesity is inconsistent and does not allow any concluded association.

subtypes of ovarian cancer are hormonally responsive, it seems logical to assume that unopposed estrogen could increase the risk of these cancers in obese women

Obesity and Cancer in Women

Cervical Cancer

Several studies have shown both increased incidence and mortality from cervical cancer among obese women.

This relationship may be because of decreased screening compliance among obese women.

Obesity is more prominent in cases of cervical adenocarcinoma than squamous cell carcinoma secondary to the role of additional estrogenic hormones.

Breast Cancer

There is a well-established link between obesity and postmenopausal breast cancer.

It is hypothesized that this is because of an increase in the serum concentration of bioavailable estradiol.

Several meta-analyses, systematic reviews, and large cohort studies havve shown obesity worsens breast cancer mortality.

Hyperinsulinemia may promote mammary carcinogenesis by increasing the levels of insulin-like growth factor and leptin.

Weight Loss and Cancer

- Cancer incidence and mortality data were compared between 6596 patients who had gastric bypass, and 9442 morbidly obese persons who had not had surgery.
- Decreased overall cancer rates in women (*P* .0004).
- Strongest impact was on endometrial cancer (*P* .0001) and with less significant impacts on premenopausal and postmenopausal breast cancer, cervical cancer and ovarian cancer

J Am Board Fam Med: first published as 10.3122/jabfm.2011.01.100076 on 5 January 2011.

Women obesity and reproduction

Reproduction

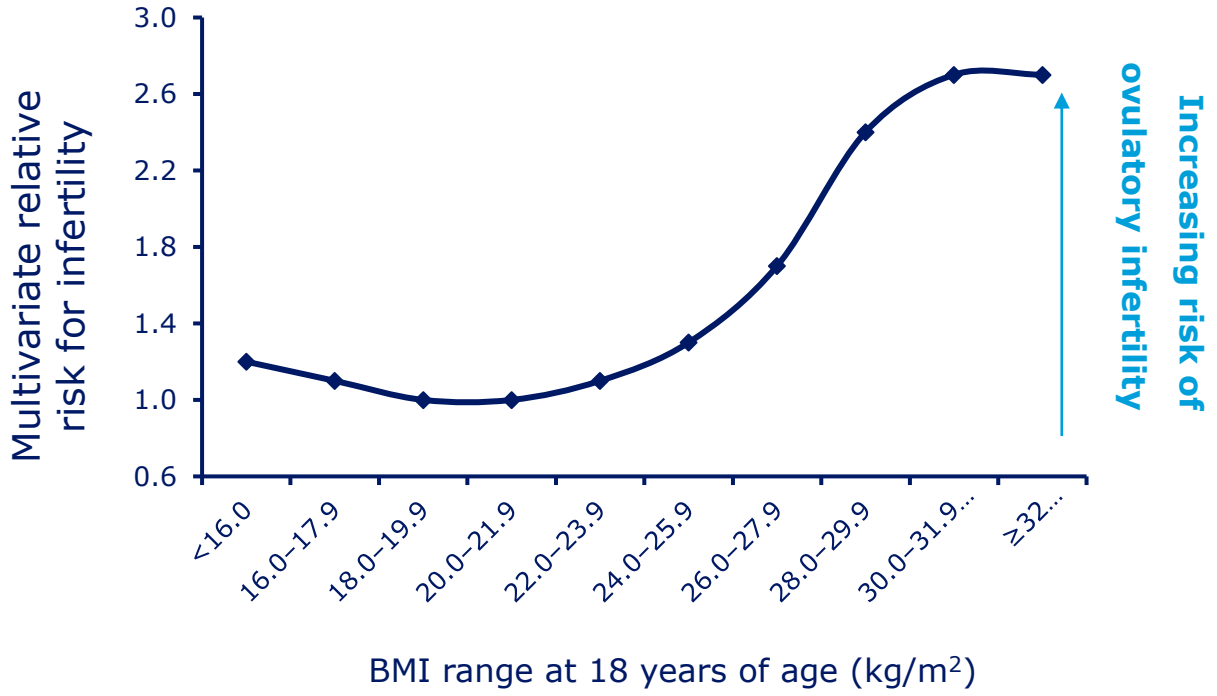
The impact of obesity on reproduction starts at a young age.

Obese girls frequently experience the onset of puberty at a younger age.

Obesity negatively affects contraception.

Hormonal contraception methods are less effective in obese women.

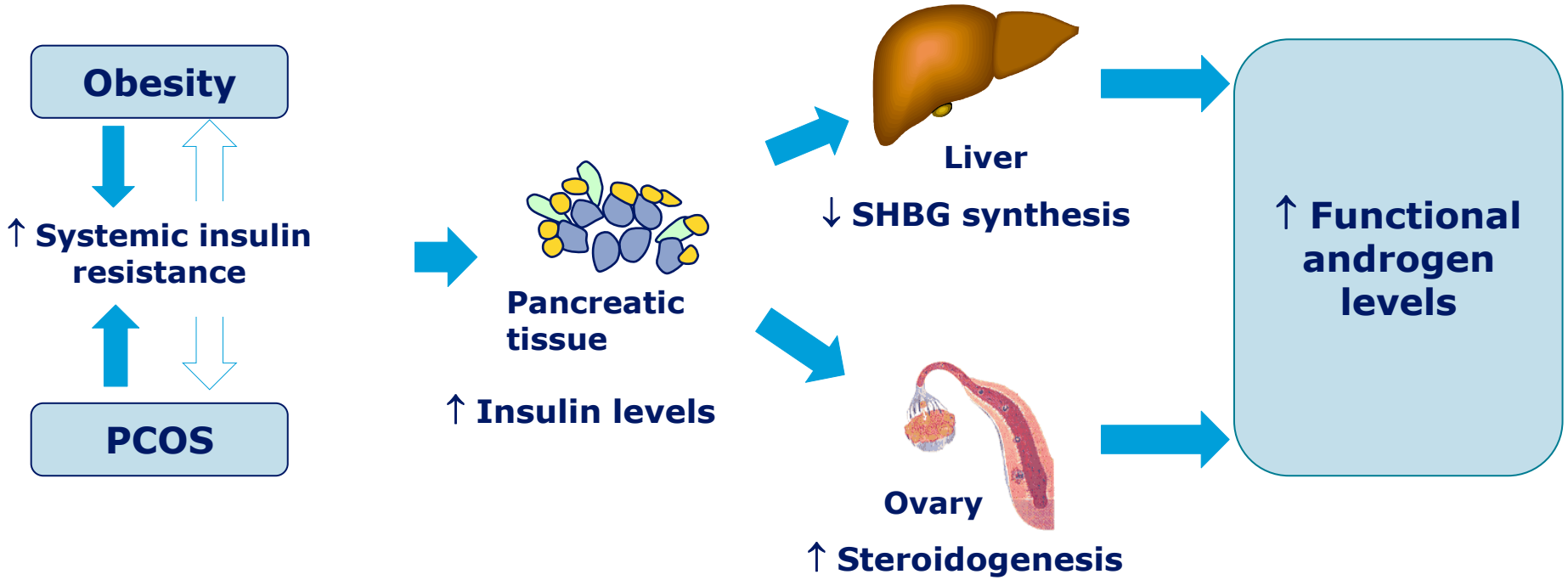
A retrospective cohort analysis of 2822 on oral contraceptive use suggested that women > 70.5 kg) had a 60% higher risk of failure than women of lower weight.



Rich-Edwards *et al. Am J Obstet Gynecol* 1994;171:171–7

Reduced female fertility in obesity is due to complex endocrine disturbances

- Complex and incompletely understood endocrine disturbances,[1,2] which include:
  - Reduced LH, FSH and oestradiol production[3]
  - Hyperandrogenism mediated via increased insulin levels[2]



FSH, follicle-stimulating hormone; LH, luteinising hormone; PCOS, polycystic ovary syndrome; SHBG, sex hormone binding globulin

1. Pasquali *et al. Hum Reprod Update* 2003;9:359–72; 2. Practice Committee of the American Society for Reproductive Medicine. *Fertil Steril* 2008;90:S21–9;
3. De Pergola *et al. Obesity* 2006;14:1954–60

Women obesity in pregnancy

Table 5. Effects of obesity on pregnancy outcomes

Condition	Type of Study
GDM (53)	Meta-analysis
PIH (54)	Meta-analysis
C-section (55)	Population-based cohort study
Pre-eclampsia (53)	Meta-analysis
Preeclampsia (56)	Retrospective cohort study
Induction of labor (56)	Retrospective cohort study
Postpartum hemorrhage (56)	Population-based cohort study
Preterm delivery (<33 weeks) (56)	Population-based cohort study
Stillbirth (57)	Systematic review and meta-anaylsis
Stillbirth (58)	Population-based cohort study
Neonatal death (58)	Population-based cohort study

Pregnancy

Obesity during pregnancy is related to higher overall health care expenditures, ,length of stay after delivery and use of other services.

Higher cesarean section rates and higher rates of high-risk obstetric conditions such as diabetes and hypertension.

The mean length of stay after delivery was directly correlated to BMI

Pre-pregnancy obesity contributes to the development of pregnancy-induced hypertension, preeclampsia, gestational diabetes, c-section, and neonatal death.

Rates of fetal anomalies are increased in obese mothers including neural tube defects, spina bifida, cardiovascular anomalies, and cleft lip and palate

Women obesity and breast feeding

Breastfeeding

Maternal obesity is associated with a decreased intention to breastfeed, decreased initiation of breastfeeding, and decreased duration of breastfeeding.

Cultural, (one's body image), or physiologic caused by metabolic and hormonal effects of adipose tissue.

Several studies have demonstrated decreased breastfeeding initiation rates among obese women.

Obese women are at greater risk of a delay in milk production

evidence that excess body fat may impair mammary gland development before conception and during pregnancy

Treatment Strategies

- The goals of obesity treatment are to reduce adiposity, decrease cardiovascular risk and mortality, and improve comorbidities and quality of life using safe, evidence-based approaches.

- Treatment strategies are in 1 of 3 therapeutic modalities, namely lifestyle, pharmacotherapy, and surgery, and in most cases multimodal combination therapy is required

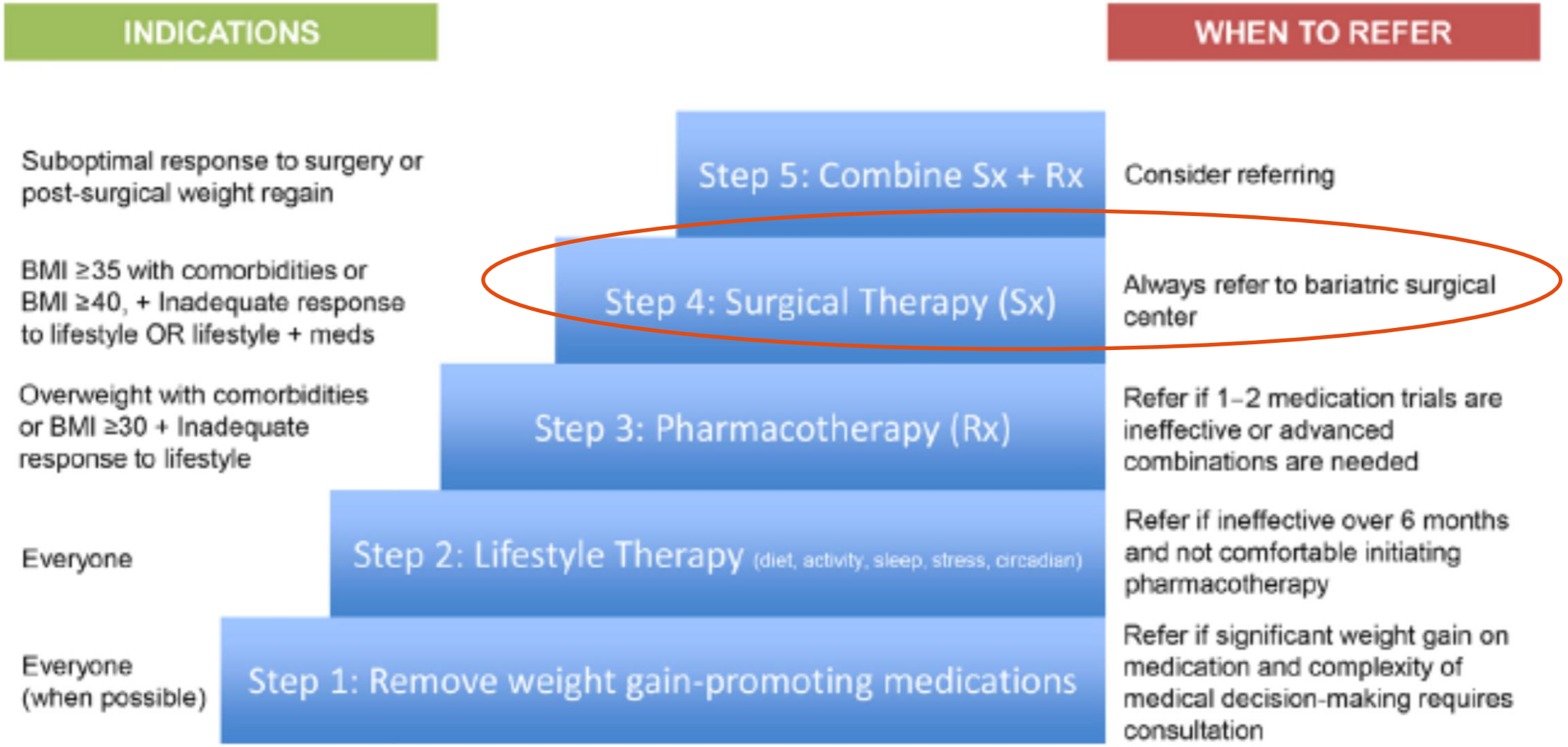


Fig. 5. Working algorithm for obesity treatment. (*Adapted from* Corey KE, Kaplan LM. Obesity and liver disease: the epidemic of the twenty-first century. Clin Liver Dis 2014;18(1):1–18.)

Table 3
Medications associated with weight gain

Weight Gain Promoting	Weight Neutral or Weight Loss Promoting
Atypical Antipsychotics	
Clozapine (Clozaril)	Ziprasidone
Olanzapine (Zyprexa)	
Quetiapine (Seroquel)	
Risperidone (Risperdal)	
Aripiprazole (Abilify)	
Haloperidol (Haldol)	
Perphenazine (Trilafon)	
Chlorpromazine (Thorazine)	
Anticonvulsants/Mood Stabilizers	
Lithium	Topiramate
Valproic acid (Valproate)	Zonisamide
Carbamazepine (Tegretol)	Lamotrigine
Vigabatrin (Sabril)	
Gabapentin (Neurontin)	
Phenytoin (Dilantin)	
Divalproex sodium (Depakote)	
Oxcarbazepine (Trileptal)	

Antidepressants	
Selective serotonin reuptake inhibitors	Bupropion
Paroxetine (Paxil)	
Citalopram (Celexa)	
Fluoxetine (Prozac)	
Sertraline (Zoloft)	
Tricyclic antidepressants	
Amitriptyline (Elavil)	
Nortriptyline (Pamelor)	
Imipramine (Tofranil)	
Monoamine oxidase inhibitors	
Phenelzine (Nardil)	
Other antidepressant	
Mirtazapine (Remeron)	
Trazadone (Desyrel)	

Antidiabetic Agents	
Insulin	Metformin
Sulfonylureas	Pramlintide
Glyburide (DiaBeta)	GLP-1 analogues
Glipizide (Glucotrol)	DPP4 inhibitors
Glimepiride (Amaryl)	SGLT-2 inhibitors
Thiazolidinediones	Acarbose
Pioglitazone (Actos)	
Rosiglitazone (Avandia)	

Antidiabetic Agents	
Insulin	Metformin
Sulfonylureas	Pramlintide
Glyburide (DiaBeta)	GLP-1 analogues
Glipizide (Glucotrol)	DPP4 inhibitors
Glimepiride (Amaryl)	SGLT-2 inhibitors
Thiazolidinediones	Acarbose
Pioglitazone (Actos)	
Rosiglitazone (Avandia)	

Antihypertensive Medications	
β-Blockers	Other antihypertensives
Propranolol (Inderal)	Carvedilol
Metoprolol (Lopressor, Toprol)	
Atenolol (Tenormin)	
α-Blockers	
Clonidine (Catapres)	
Prazosin (Minipress)	
Terazosin (Hytrin)	

Weight Gain Promoting	Weight Neutral or Weight Loss Promoting
Corticosteroids	
Prednisone Hydrocortisone Dexamethasone	Cytotoxic agents
Antihistamines	
Diphenhydramine (Benadryl)	Loratadine
Hormonal Contraceptives	
Depo-medroxyprogesterone acetate (Depo-Provera) **Oral contraceptives** Hormonal intrauterine device Hormone vaginal ring	Nonhormonal contraception
Sleep Aids	
Zolpidem	Melatonin Sleep hygiene counseling

PHARMACOTHERAPY

According to clinical guidelines:

- Pharmacotherapy for obesity is recommended for a BMI greater than 30 kg/m2 or BMI greater than 27 kg/m2 with obesity-related comorbidities.
- Lifestyle change should have been attempted and yielded inadequate results before starting an anti-obesity medication.
- Pharmacotherapy in conjunction with, rather than after, lifestyle changes

- Aim for a double benefit, such as the use of topiramate in the presence of migraines, or metformin in PCOS.
- To minimize side effects while maximizing efficacy, slow-titration regimens and combination treatments are recommended.
- long-term therapy is recommended

Bariatric surgery

- Weight loss surgery for obesity is recommended for individuals with a BMI greater than or equal to 40, or BMI greater than or equal to 35 and obesity-related comorbidities.
- Comorbidities : type 2 diabetes, PCOS, hypertension, sleep apnea and other respiratory disorders, nonalcoholic fatty liver disease, osteoarthritis, lipid abnormalities, gastrointestinal disorders, heart disease, or infertility.
- It is recommended that pregnancy be avoided in the initial weight loss phase up to 18 months after the procedure.
- Bariatric surgery has been found to have positive effects on PCOS and infertility


Thank
You