

**31 MAIO
A 2 JUN
2018**

XIX CONGRESSO SUL-BRASILEIRO
DE GINECOLOGIA E OBSTETRÍCIA
IV JORNADA SUL-BRASILEIRA
DE MASTOLOGIA



MESA REDONDA 15: "Hiperandrogenismo feminino, como tratar?"

Presidente de Mesa: DRA. IVANA FERNADES SOUZA (FLORIANÓPOLIS/SC - Brasil)

Alopécia

Palestrante: DR. MARCELO RIGATTI (FLORIANÓPOLIS/SC - Brasil)

Hirsutismo

Palestrante: DR. JAIME KULAK JUNIOR - SOG/PA (CURITIBA/PR - Brasil)

Obesidade

Palestrante: DRA. LILIANE DIEFENTHAELER HERTER (PORTO ALEGRE/RS - Brasil)

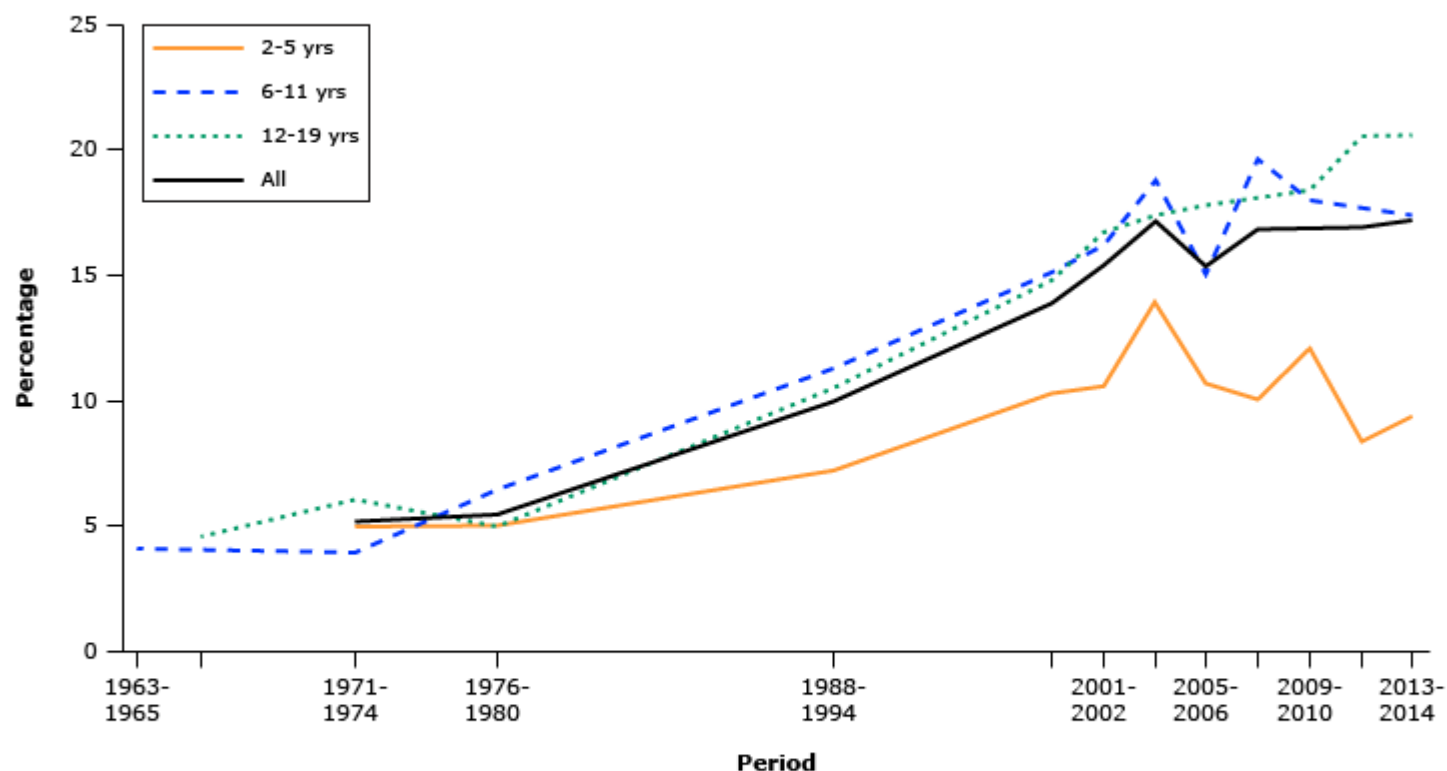


UFCSPA

Declaro ausência de conflito de interesse

Liliane Diefenthaeler Herter

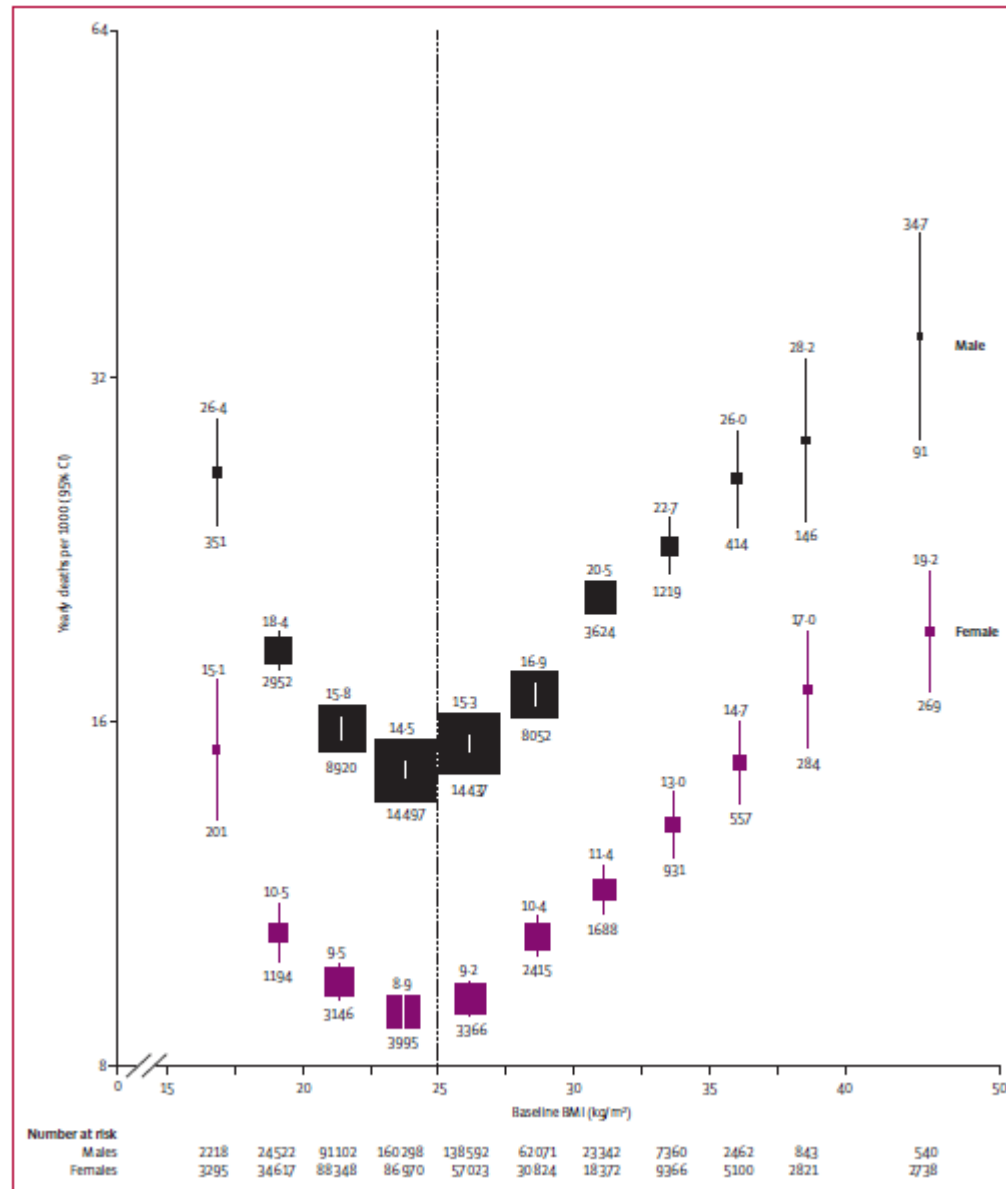
Trends in obesity among children and adolescents aged 2–19 years, by age: United States, 1963–1965 through 2013–2014



Data from the United States Health and Nutrition Examination Surveys (NHANES). Obesity is defined as a body mass index (BMI) ≥ 95 th percentile for age and gender. This figure does not distinguish between groups with mild versus severe obesity.

Fryar CD, Carroll MD, and Ogden CL. Prevalence of Overweight and Obesity Among Children and Adolescents Aged 2–19 Years: United States, 1963–1965 Through 2013–2014. *Health E-Stats* July 2016. Available at:

Figure 2: All-cause mortality versus BMI for each sex in the range 15–50 kg/m² (excluding the first 5 years of follow-up)



OBESIDADE

CONCEITO EM ADULTOS:

- Normal: IMC 18 – 24,9 kg/m²
- Sobrepeso: IMC 25 – 29,9 kg/m²
- Obesidade: IMC \geq 30 kg/m²
 - Obesidade grave (I): 30 – 34,9 kg/m²
 - Obesidade moderada (II): 35 – 39,9 kg/m²
 - Obesidade grave (III): \geq 40 kg/m²

OBESIDADE

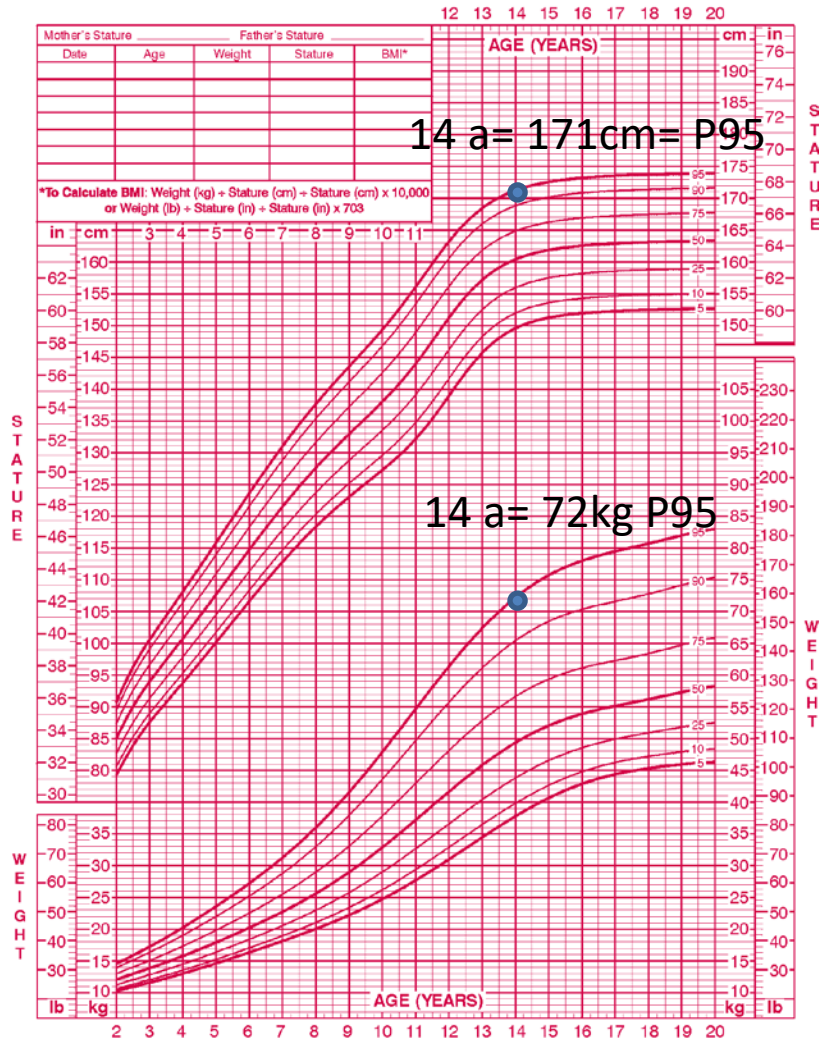
CONCEITO EM ADOLESCENTES:

- **Sobrepeso:** **IMC = Perc 85- 94,9**
- **Obesidade:** **IMC \geq Perc 95**
- **Obesidade grave:** **IMC \geq Perc 99**

2 to 20 years: Girls
Stature-for-age and Weight-for-age percentiles

NAME _____

RECORD # _____



Published May 30, 2000 (modified 11/21/00).
SOURCE: Developed by the National Center for Health Statistics in collaboration with
the National Center for Chronic Disease Prevention and Health Promotion (2000).
<http://www.cdc.gov/growthcharts>

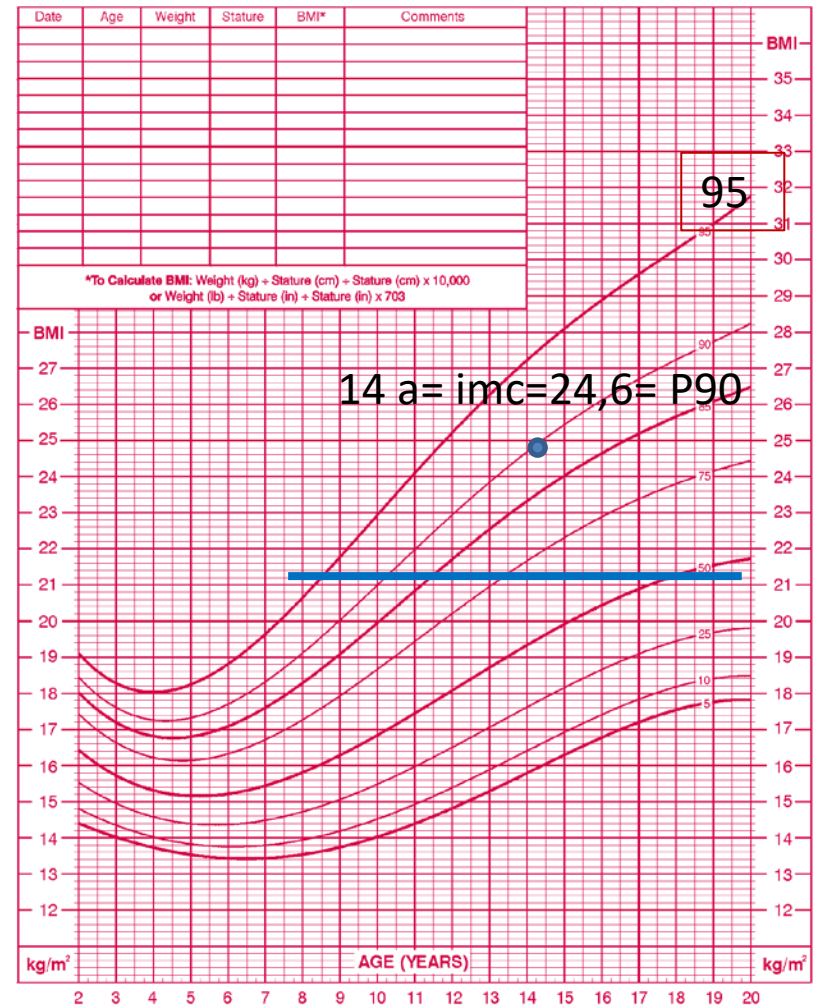


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2 to 20 years: Girls
Body mass index-for-age percentiles

NAME _____

RECORD # _____



Published May 30, 2000 (modified 10/15/00).
SOURCE: Developed by the National Center for Health Statistics in collaboration with
the National Center for Chronic Disease Prevention and Health Promotion (2000).
<http://www.cdc.gov/growthcharts>



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MEDIDA DA CINTURA

MULHERES

- ≥ 88 cm em adultas americanas
- ≥ 80 cm em adultas europeias

HOMENS

- ≥ 102 cm em adultos americanas
- ≥ 94 cm em adultos europeus

AUMENTA RISCO DE DOENÇA CARDIOMETABÓLICA

OBESIDADE

- Resistência Insulínica
- Inflamação crônica
- Disfunção vascular
- Alterações no metabolismo dos lipídios
- Alterações no metabolismo dos carboidratos

OBESIDADE

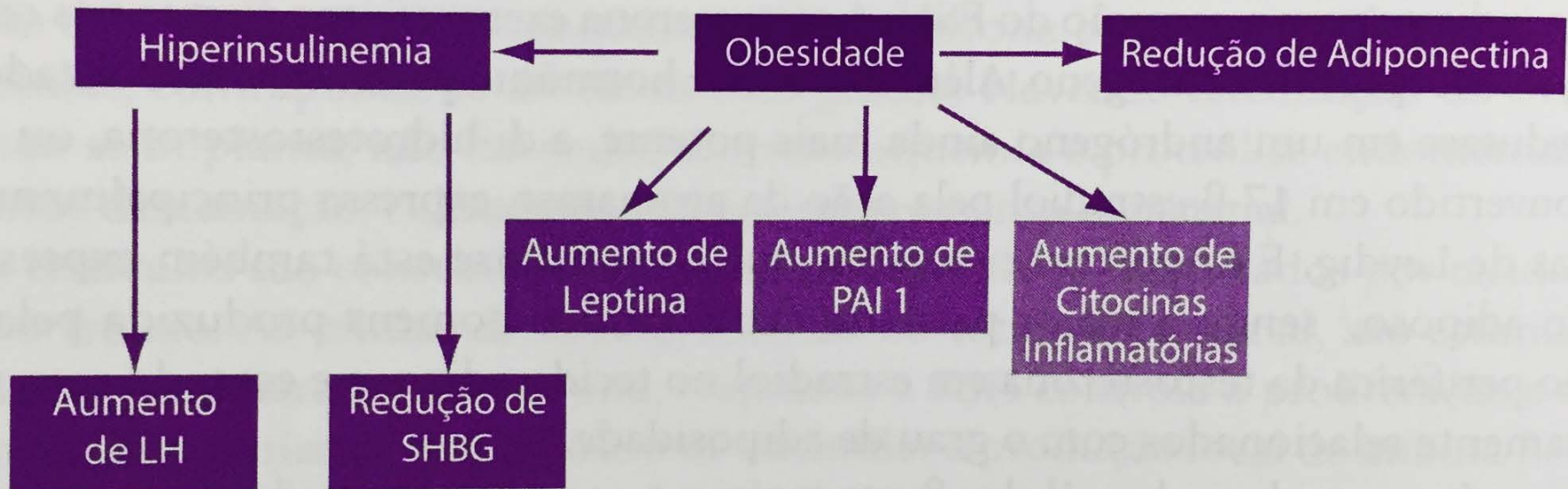
FATOR DE RISCO PARA:

- DM 2
- Dislipidemia
- HAS
- Doença cardiovascular
- Câncer
- Apnéia do sono
- Esteatose hepática
- Hiperandrogenismo
- Adiantamento da puberdade

TECIDO ADIPOSEO

- É um órgão endócrino capaz de sintetizar e secretar substâncias envolvidas na:
 - Fisiopatogênese da resistência à insulina
 - Inflamação sistêmica
 - Aterogênese
- Produz adipocinas:
 - **Leptina** (homeostase energética, sensibiliza Insulina, tem propriedades proliferativas e aterogênicas)
 - **Adiponectina** (potente anti-inflamatório tecidual; atenua a RI hepática, a inflamação e fibrose hepática)

ALTERAÇÕES ENDOCRINO-INFLAMATÓRIAS INDUZIDAS PELA OBESIDADE

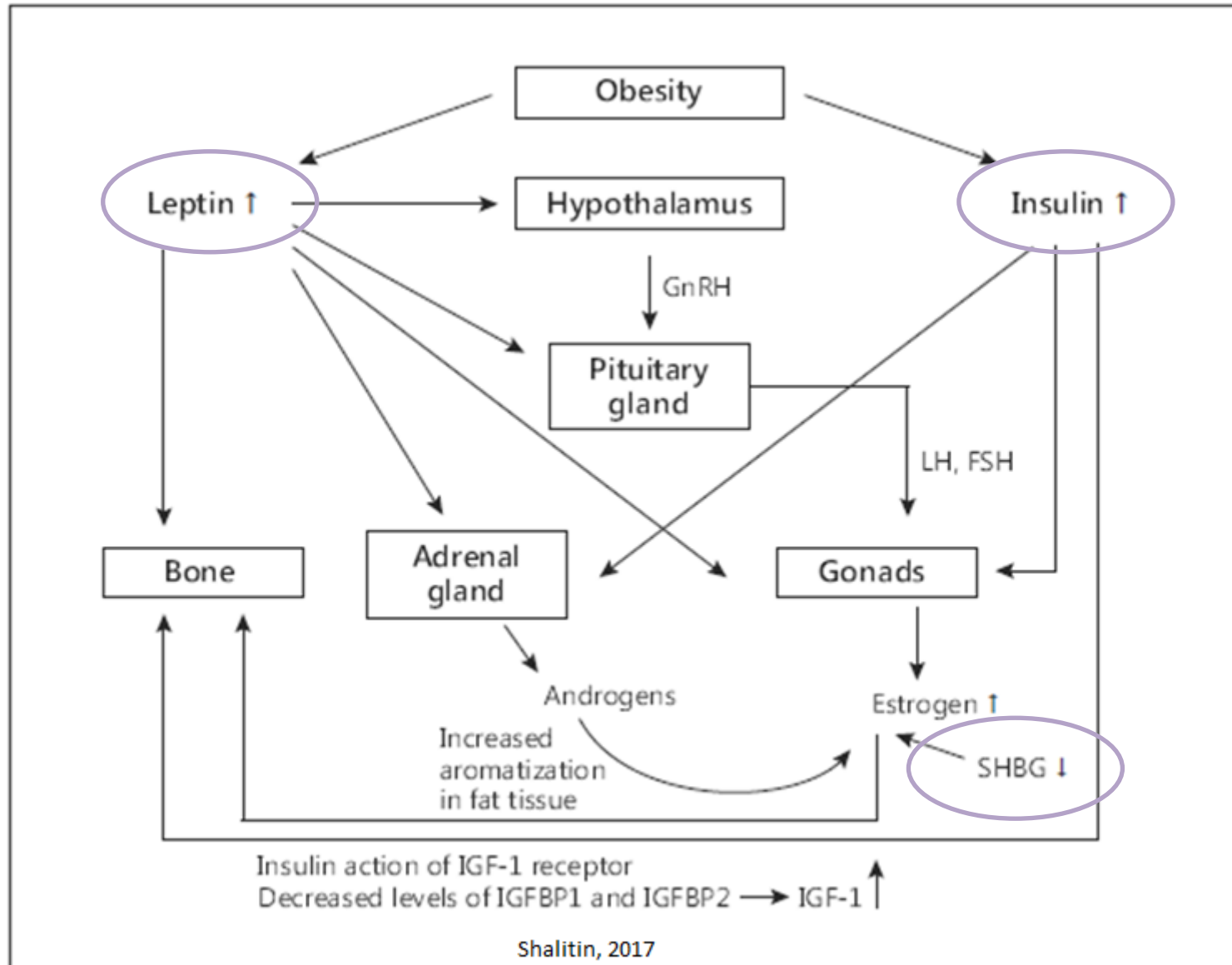


Ruth Clapauch , Endocrinologia Feminina e Andrologia, 2012

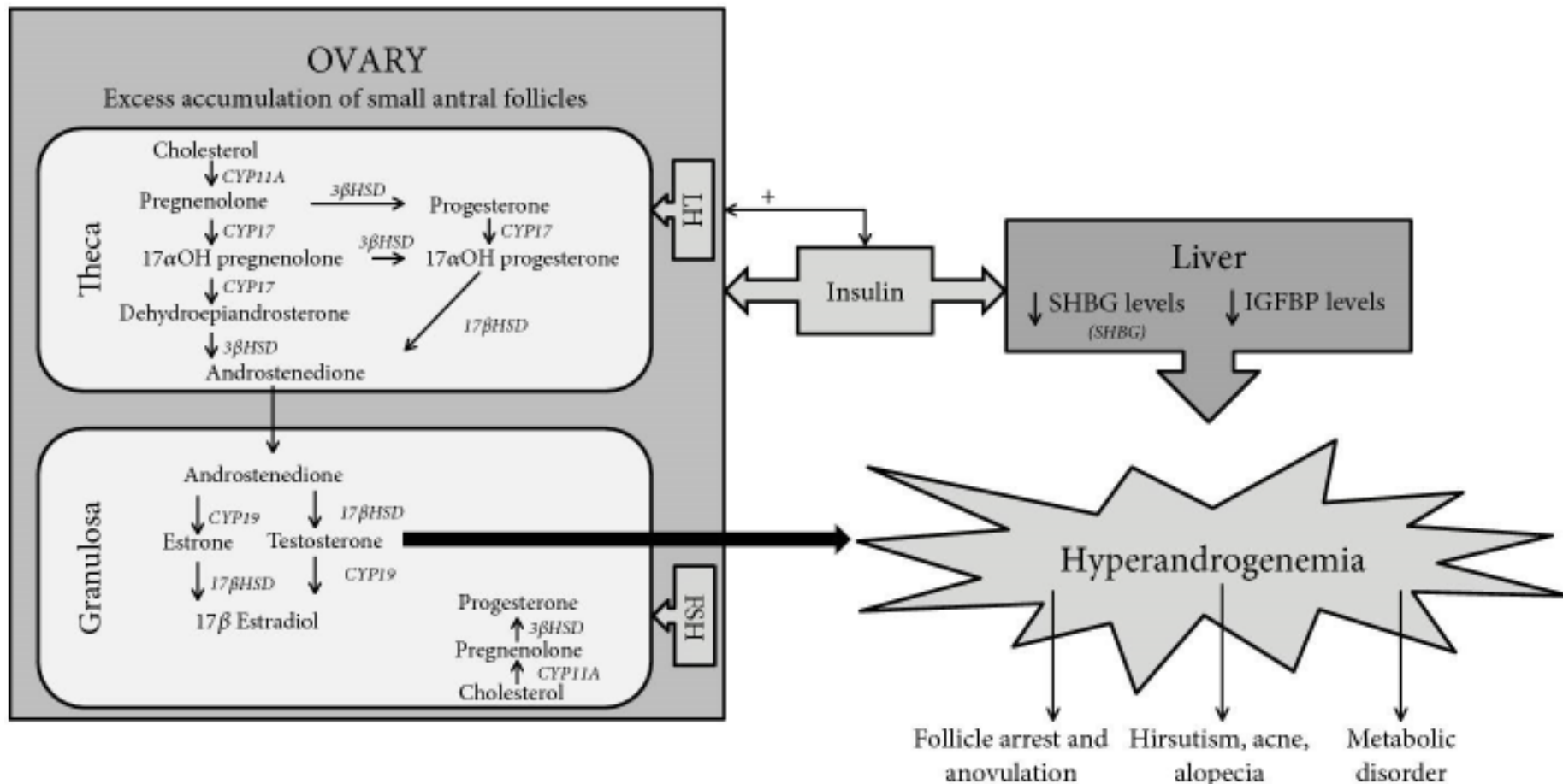
ALTERAÇÕES HORMONAIS NA OBESIDADE

HORMÔNIOS	MULHER
FSH	N / ↓
LH	↑
SHBG	↓
TESTOTERONA	↑
ESTRADIOL	↑
PROGESTERONA	↓

OBESIDADE x ANTECIPAÇÃO DA PUBERDADE



OVERVIEW OF PATHOPHYSIOLOGY OF PCOS



Gynecologic and Obstetric Consequences of Obesity in Adolescent Girls



Leticia Elizondo-Montemayor MD ^{1,*}, Claudia Hernández-Escobar MD ¹, Eduardo Lara-Torre MD ², Bianca Nieblas BSc ¹, Merith Gómez-Carmona MD ¹

¹ Tecnológico de Monterrey, Escuela de Medicina, Monterrey, Nuevo Leon, México

² Carilion Clinic, Virginia Tech-Carilion School of Medicine, Roanoke, Virginia

ABSTRACT

In the past few decades, there has been an overwhelming increase in childhood and adolescent obesity worldwide. Besides the well recognized cardiometabolic complications and other physical conditions associated with obesity, during adolescence, it causes psychological and social distress in a period of life that is already sensitive for a girl. This in turn increases their risk of low self-esteem and depression. Furthermore, obesity diminishes health-related quality of life and years of life. Overweight and obese teenagers are more likely to have gynecologic and obstetric complications, during adolescence and also later in life. Consequences of obese and overweight childhood and adolescence include sexual maturation and reproductive dysfunction, alterations in menstruation, dysmenorrhea, risky sexual behavior, and inefficient use of contraception, polycystic ovary syndrome, bone density abnormalities, macromastia, and an increased risk of breast and endometrial cancer. Obese adolescents are at greater risk of pregnancy and perinatal complications, such as preeclampsia, gestational hypertension and preeclampsia, gestational diabetes mellitus, primary cesarean delivery, and induction of labor, to mention a few. Evidence shows that infants born to obese teenagers are also more likely to have complications including preterm or post-term delivery, small-for-gestational age newborns, macrosomia, meconium aspiration, respiratory distress, and even stillbirth, among others. This comprehensive review focuses on the gynecological and obstetric consequences of obesity in adolescent girls.

Key Words: Obesity, Adolescents, Girls, Gynecologic, Obstetric, Sexual maturation, Puberty, Pregnancy, Reproductive function, Polycystic ovary syndrome

Table 2
Gynecological Consequences of Obesity in Adolescent Girls

Consequences	Effect	Mechanisms Involved
Puberty	Earlier onset of puberty	Insulin resistance, hyperandrogenism, altered HPA, higher levels of leptin and kisspeptin, and endocrine disruptive chemicals
Reproductive function	Reduced fertility Less likely to accomplish spontaneous pregnancy or to achieve pregnancy or live birth with assisted reproductive technologies	Longer follicular phases, shorter luteal phases, lower FSH, and progesterone levels Alterations of follicle development, oocyte quality, and endometrial receptivity Leptin and adiponectin involved
Disorders of menstruation	Twice as likely to have irregular menstruations Predisposes to PCOS and infertility	Increased aromatization, ovarian volume, testosterone, LH, and insulin
Dysmenorrhea	A U-shaped association revealed a greater risk of dysmenorrhea for underweight and obese	Reduced concentrations of SHBG
Sexual behavior	Greater risk for unsafe sexual behavior Less likely to be sexually active	Fear that hormones might contribute further to weight gain
Contraception	Less use of contraceptives, and Increased risk of pregnancy Most studies affirm weight gain except with low dose COC	Obesity affects pharmacokinetics of COC, modifying bioavailability, metabolism, and clearance of drugs
PCOS	Increased risk of PCOS Severity of PCOS intensified Increased risk of MetS	Increased levels of insulin, IGF-1, LH, and androgens, and conversion to testosterone Decreased SHBG
Mineralization and bone density	Controversial Obesity decreases BMC and BMD; worse if cardiometabolic factors are present Some studies show no association	Adipokines, particularly IL-6 and TNF hamper bone formation and reabsorption Failure to adjust bone development with excess weight
Macromastia	Greater prevalence Lower HRQOL and self-esteem Greater risk of eating disorders	Increased demand for breast reduction
Breast cancer	Greater BMI, earlier puberty, and heavier birth weight increase risk	Overexpression of aromatase, increased levels of insulin, IGF-1, IL-4, IL-6, leptin, and resistin affect tumorigenesis
Endometrial cancer	Increased risk for postmenopausal but not premenopausal Endometrial atypia hyperplasia and cancer are uncommon Obesity during adolescence increases risk of cancer later in life	Chronic anovulation increases risk due to the effect of unopposed estrogens Earlier onset of puberty increases risk of cancer in adulthood

BMC, bone mineral content; BMD, bone mineral density; BMI, body mass index; COC, combined oral contraceptives; FSH, follicular stimulating hormone; HPA, hypothalamic-pituitary-adrenal; HRQOL, health-related quality of life; IGF-1, insulin like growth factor-1; IL, interleukin; LH, luteinizing hormone; MetS, metabolic syndrome; PCOS, polycystic ovary syndrome; SHBG, sexual hormone binding globulin; TNF, tumor necrosis factor

CONSEQUÊNCIAS NA FUNÇÃO REPRODUTIVA DA MULHER

- Altera pulsatilidade do GnRH
- Altera foliculigênese e esteirodogênese ovariana
- Altera a irrigação próxima ao folículo
- Interfere no desenvolvimento endometrial
- Induz regressão do corpo lúteo
- Causa hipercoagulabilidade (↑ Inibidor do ativador do plasminogênio tipo 1= PAI-1)

HIPERANDROGENISMO

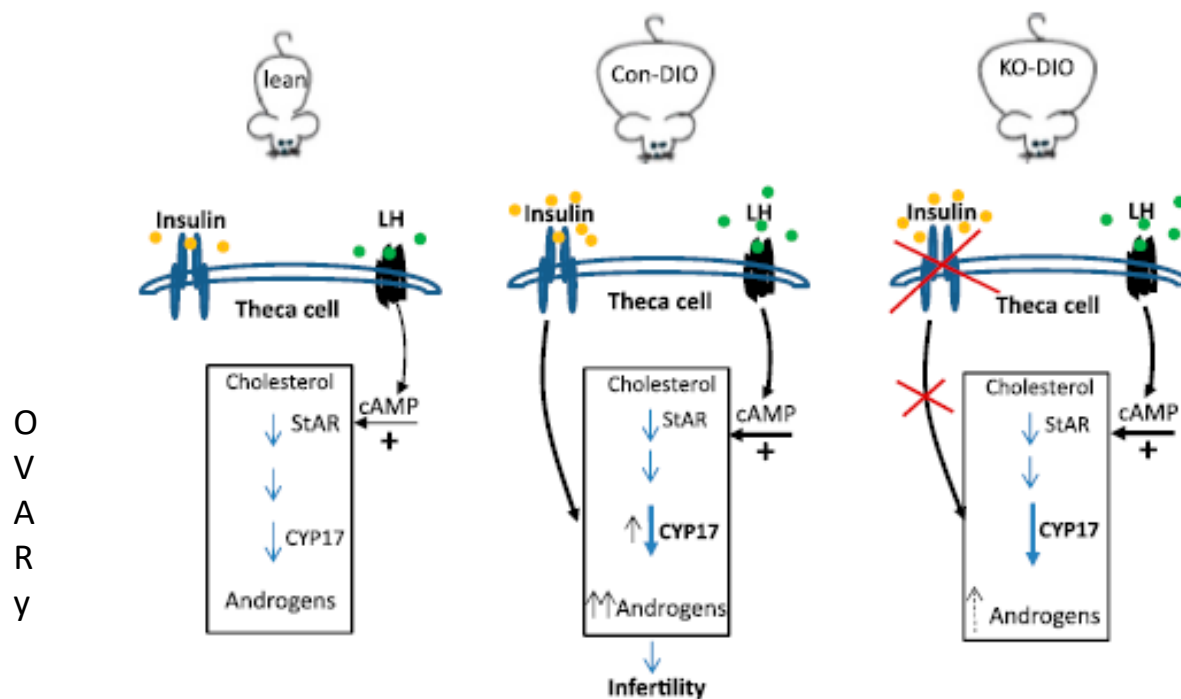
- Hirsutismo
- Alopecia / seborréia
- Acne moderada-grave
- Hidradenite supurativa
- Pubarca precoce
- Virilização

OBESIDADE X HIPERANDROGENISMO

- Obesidade ocorre em **50% das SOP**
- Obesidade **pode exacerbar** os distúrbios metabólicos e reprodutivos associados com a SOP (Spritzer, 2014)
 - Resistência Insulínica
 - Dislipidemia
 - Síndrome metabólica

Obesity-Induced Infertility and Hyperandrogenism Are Corrected by Deletion of the Insulin Receptor in the Ovarian Theca Cell

Sheng Wu et al



- In **lean mice**, LH is a major resource to trigger androgen secretion in TI cells of the ovary.
- In **DIO mice**, insulin and LH both induce androgen production by increasing the Cyp17 protein level.
- Without IR, the KO-DIO mice have attenuated androgen production and improved fertility compared with the control (Con)-DIO mice.

KO= Cyp17IR knockout mice (Cyp17IRKO) **DIO**= Diet-induced obesity female mice **Con**= control

Hepatic Steatosis is Common in Adolescents with Obesity and PCOS and Relates to *De Novo* Lipogenesis but not Insulin Resistance

Melanie Cree-Green^{1,2}, Bryan C. Bergman³, Gregory V. Coe¹, Lindsey Newnes¹, Amy D. Baumgartner¹, Samantha Bacon³, Ann Sherzinger⁴, Laura Pyle^{5,6}, and Kristen J. Nadeau^{1,2}

Esteatose Hepática:

49% PCOS-Obese Adolescent x 14% Obese Adolescent (P=0,02)

Objective

drome (PCOS) and insulin resistance (IR) in girls with obesity.

Methods

35.2 ± 0.6 years, BMI 35.2 ± 0.6, visceral and subcutaneous fatty acid oxidation rates were assessed.

Results:

group (P=0.006) and

was lower (P=0.006) and

0.006) and

fat (R = 0.49).

Conclusion

relates to visceral fat and lipogenesis, but not to IS or androgens.

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adoles-
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TRATAMENTO

- Aconselhamento de risco
- Dieta
- Exercício
- Mudança do estilo de vida
- Medicação
- Cirurgia
- Psicoterapia

TRATAMENTO

- **RISCO PEQUENO OU NULO:**

- Aconselhar não aumentar de IMC 25

- **RISCO BAIXO:**

- Aconselhar dieta , exercício físico e mudança de estilo de vida

- **RISCO MODERADO:**

- Aconselhar dieta , exercício físico e mudança de estilo de vida
- e **tratamento medicamentoso** na falha destes

- **RISCO ALTO:**

- Aconselhar dieta , exercício físico e mudança de estilo de vida e **tratamento medicamentoso** na falha destes

- **RISCO MUITO ALTO:**

Aconselhar dieta , exercício físico e mudança de estilo de vida e tratamento medicamentoso. **Cirurgia** na falha destes

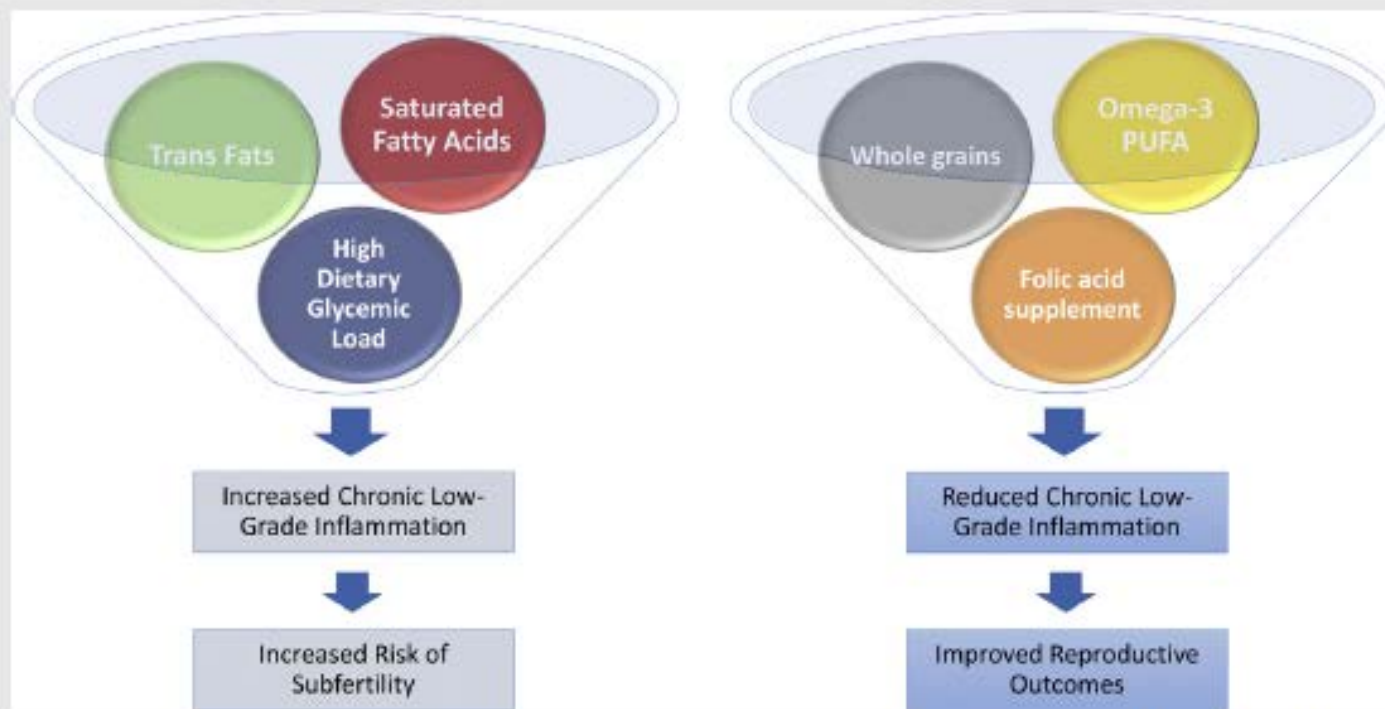
OBJETIVO

- Perda de peso: $\geq 5 - 10 \%$

DIETA

- Hipocalórica (800 – 1200 kcal/dia)
 - Low fat/low calorie
 - Low carbho
 - Dieta mediterrânea
 - Dieta paleolítica

Is there a role for diet in ameliorating the reproductive sequelae associated with chronic low-grade inflammation in polycystic ovary syndrome and obesity?



Women with polycystic ovary syndrome or that are obese seeking fertility treatment may benefit from lifestyle interventions. Alterations in dietary intake of fats, carbohydrates, and proteins may mitigate the low-grade chronic inflammation associated with these disorders and improve fertility.

Riley. *Inflammation and diet in PCOS and obesity?* *Fertil Steril* 2016.

Riley et al. *Fertil Steril* **2016**;106:520–7.

DIETAS : carboidratos

- Dieta com alta ingestão de carboidratos e alta carga glicêmica= ↑ risco de infertilidade
- Dietas com baixo índice glicêmico= ↓ marcadores inflamatórios (ex: PCR)
- Em pacientes com FIV, dietas pré-tratamento com maior oferta de grãos= ↑ taxas de nascidos vivos

DIETAS: gorduras

- ↑ Gordura trans=
 - ↑ Infertilidade
 - ↑ Resistência Insulínica
 - ↑ Estado inflamatório
- Carne de gado e frango são ricos em ácido aracdônico (ácido graxo proinflamatório)

Riley et al. Fertil Steril 2016;106:520–7.

PRESCRIÇÃO DIETÉTICA

reduzir o status inflamatório

- **Reduzir excesso de CH**
- Preferir alimentos com **baixo índice glicêmico**
- **Evitar CH refinados**
- Introduzir **grãos / integrais**
- **Reduzir gordura trans** (margarina, óleos vegetais). Preferir **azeite oliva extra-virgem , manteiga, óleo de coco virgem.**
- Estimular a troca de carne de gado e galinha por **proteínas vegetais ou carne de salmão (rico em omega 3)**
- **Suplementação com omega 3 de cadeia longa** pode melhorar perfil hormonal e metabólico em SOP

EXERCÍCIO

- ≥ 30 minutos
- ≥ 5 x semana

MUDANÇA DE ESTILO DE VIDA

- Redução de estressores
- Redução de gatilhos
- Métodos comportamentais

MELHOR TRATAMENTO PARA OBESIDADE

DIETA

+

ATIVIDADE FÍSICA

+

MÉTODOS COMPORTAMENTAIS

MEDICAÇÃO

IMC > 30 kg/m²

IMC > 25 kg/m² com comorbidades

Falha na perda de 5% IMC/6 meses

- Orlistat (Xenical[®])
- Liraglutide SC (Victoza[®])
- Topiramato (Topamax[®])
- Bupropiona (Zetron[®])
- Naltrexona (Revia[®])
- Lorcaserina (Lorqess)
- Anfepramona (Hipofagin)
- Femproporex (Perphoxene)
- Sibutramina (Reductil[®])
- Metformina (Glifage[®])

TABELA 8.4 Principais medicações utilizadas para o tratamento da obesidade

Medicação	Mecanismo de ação	Dose habitual	Efeitos colaterais
Sibutramina	Inibe a recaptação de serotonina e da noradrenalina	10-15 mg/dia	Boca seca, aumento da pressão arterial e frequência cardíaca, constipação
Orlistat	Reduz a absorção de gordura no intestino (em torno de 30%)	120-360 mg/dia	Diarreia, flatulência, dispepsia
Fluoxetina*	Inibe a recaptação de serotonina	10-60 mg/dia	Nervosismo, náuseas, redução da libido
Topiramato*	Atua na modulação de receptores do ácido gama-amino-butírico	75-200 mg/dia	Problemas de coordenação, dificuldade de concentração, tontura, parestesias
Bupropiona*	Inibe recaptação de dopamina e noradrenalina	150-300 mg/dia	Convulsões, insônia, tremor, distúrbios de concentração

Effectiveness of Primary Care–Relevant Treatments for Obesity in Adults: A Systematic Evidence Review for the U.S. Preventive Services Task Force

Erin S. LeBlanc, MD, MPH; Elizabeth O'Connor, PhD; Evelyn P. Whitlock, MD, MPH; Carrie D. Patnode, PhD, MPH; and Tanya Kapka, MD, MPH

Background: Overweight and obesity in adults are common and adversely affect health.

Purpose: To summarize effectiveness and harms of primary care–relevant weight-loss interventions for overweight and obese adults.

Data Sources: MEDLINE, Cochrane Central Register of Controlled Trials, and PsycINFO from January 2005 to September 2010; systematic reviews for identifying trials before 2005.

Study Selection: Two investigators appraised 6498 abstracts and 648 articles. Clinical trials were included if control groups received minimal interventions. Articles were rated as good, fair, or poor by using design-specific criteria.

Data Extraction: One investigator abstracted study characteristics and findings for good- and fair-quality studies; a second checked them.

Data Synthesis: Behaviorally based treatment resulted in 3-kg (6.6-lb) greater weight loss in intervention than control participants after 12 to 18 months, with more treatment sessions associated with greater loss. Limited data suggest weight-loss maintenance for 1 year or more. Orlistat plus behavioral intervention resulted in 3-kg (6.6-lb) more weight loss than did placebo after 12 months. Met-

formin resulted in less weight loss. Data on effects of weight-loss treatment on long-term health outcomes (for example, death and cardiovascular disease) were insufficient. Weight-loss treatment reduced diabetes incidence in participants with prediabetes. Effects on intermediate outcomes (for example, lipids and blood pressure) were mixed and small. Data on serious medication harms were insufficient. Medications commonly caused withdrawals due to gastrointestinal symptoms.

Limitations: Few studies reported health outcomes. Behaviorally based treatments were heterogeneous and specific elements were not well-described. Many studies could not be pooled because of insufficient reporting of variance data. Medication trials had high attrition, lacked postdiscontinuation data, and were inadequately powered for rare adverse effects.

Conclusion: Behaviorally based treatments are safe and effective for weight loss and maintenance.

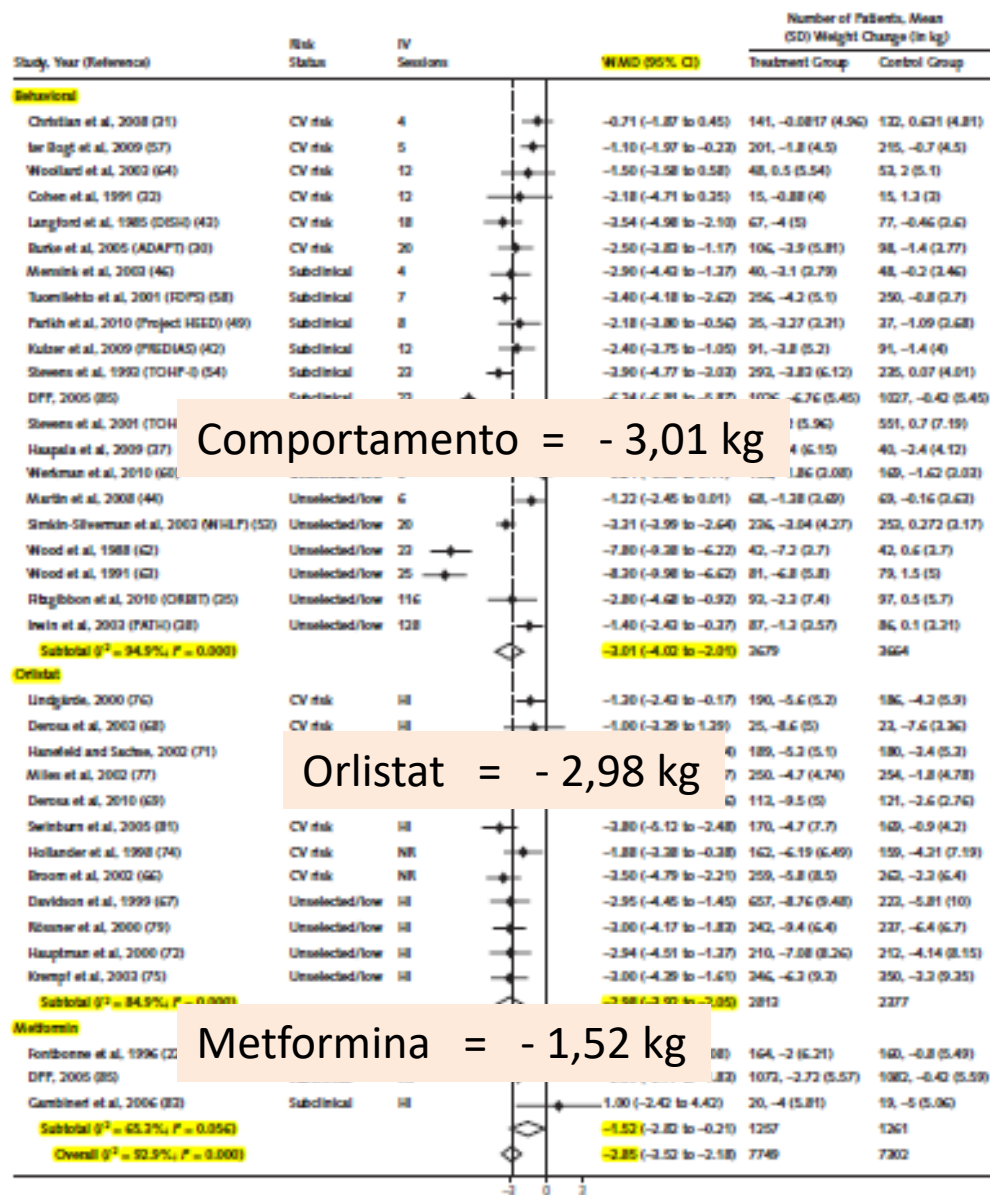
Primary Funding Source: Agency for Healthcare Research and Quality.

Ann Intern Med. 2011;155:434-447.

For author affiliations, see end of text.

www.annals.org

Figure 1. Difference between intervention and control groups in weight change at 12 to 18 months.



Weights are from random-effects analysis. ADAPT = Activity, Diet and Blood Pressure Trial; CV = cardiovascular; DISH = Dietary Intervention to Study Hypertension; DPP = Diabetes Prevention Program; FDP5 = Finnish Diabetes Prevention Study; HEED = Help Educate to Eliminate Diabetes; HI = intensive intervention; IV = intervention; LO = brief intervention; NR = not reported; ORBIT = Obesity Reduction Black Intervention Trial; PATH = Physical Activity for Total Health; PREDIAS = Prevention of Diabetes Self-Management Program; Subclinical = trials limited to those with elevated risk but without known disease (prehypertension; impaired glucose tolerance or elevated fasting glucose; borderline high total cholesterol, low-density lipoprotein, or triglyceride levels; low high-density lipoprotein levels; abdominal obesity); TOHP = Trials of Hypertension Prevention; WHLP = Women's Healthy Lifestyle Project; WMD = weighted mean difference.

RESISTÊNCIA INSULÍNICA

- É comum mas não obrigatória na SOP
- Uso de sensibilizadores da insulina se:
 - Acanthosis nigricans
 - Obesidade total e central
 - Glicemia basal ≥ 100 mg/dL
 - TTG glicemia 2h ≥ 140 mg/dL
 - Diabetes tipo 2

TRATAMENTO CIRÚRGICO

- IMC 35 – 40 kg/m² com comorbidades
- IMC \geq 40 kg/m²

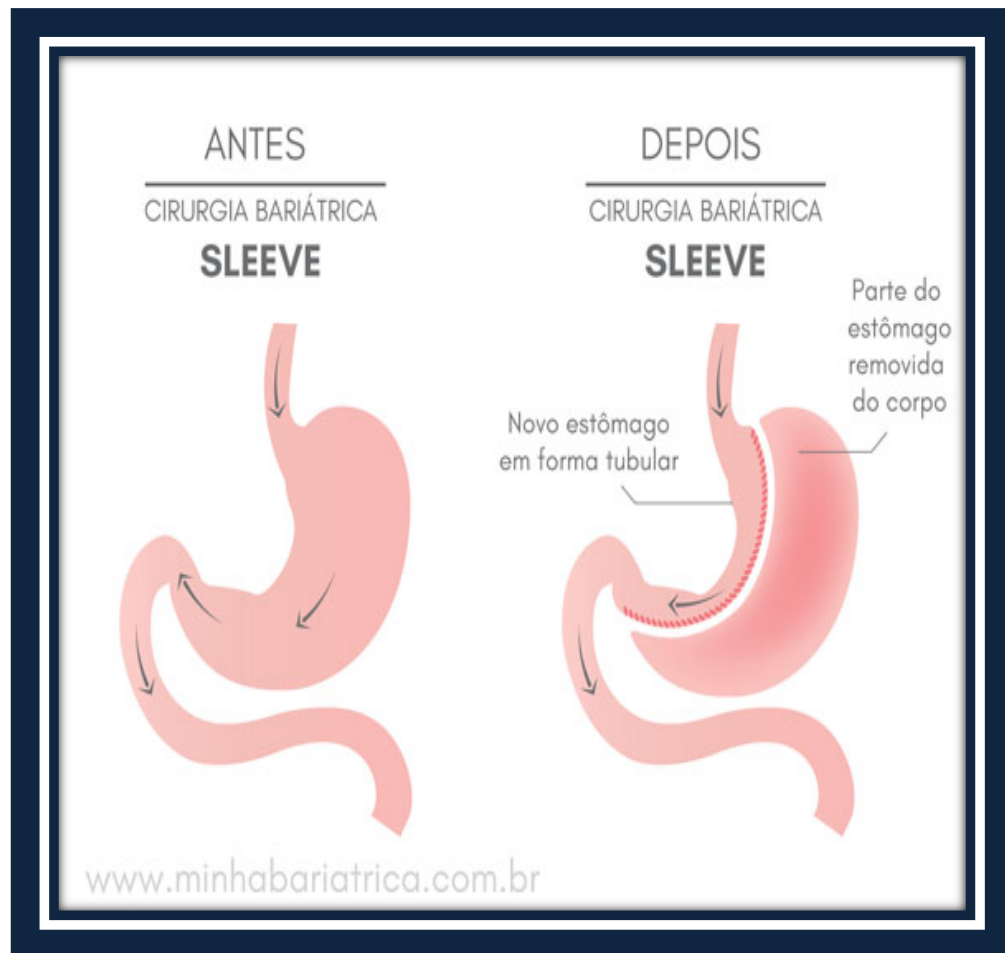
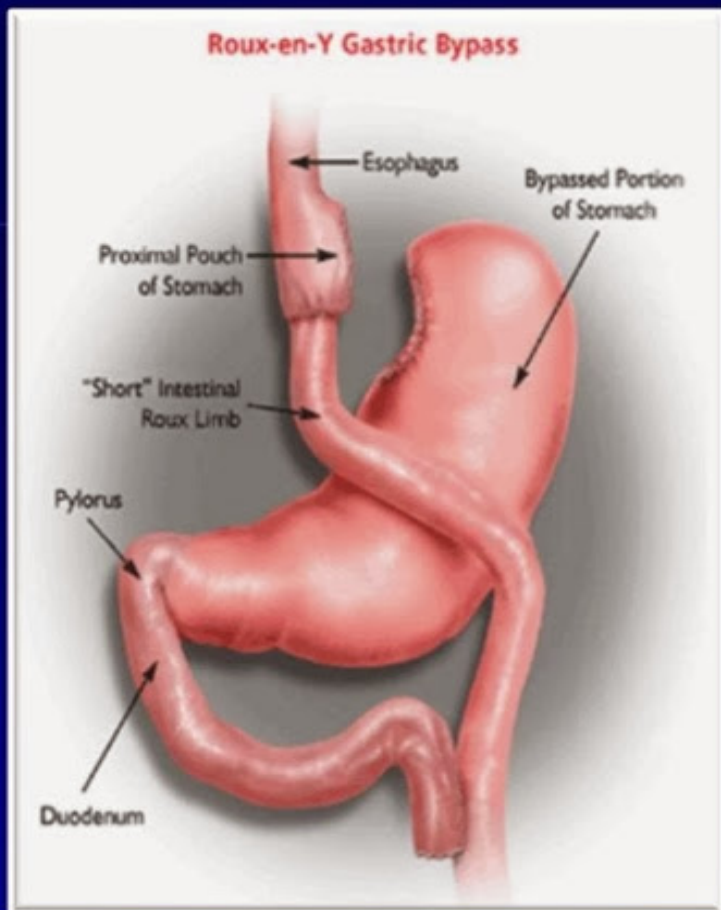
CENTRO DE TRATAMENTO DA OBESIDADE

SANTA CASA DE PORTO ALEGRE

2004 - 2018

- **CIRURGIAS REALIZADAS:** 2340
 - 64% by pass
 - 36% sleeve (2008)
- **SEXO:**
 - 74% feminino
 - 26% masculino
- **COMPLICAÇÕES :**
 - 6,5% (literatura 8 - 10%)
- **MORTALIDADE:**
 - 0,2% (literatura 0,5%)

TÉCNICAS MAIS FREQUENTES



CONCLUSÃO

- Obesidade está relacionada com:
 - Desfechos negativos para saúde e para fertilidade
 - É um estado crônico de:
 - Hiperandrogenismo
 - Inflamação crônica
 - É um gatilho para a SOP
- Tratamento inclui tto em equipe multidisciplinar:
 - Dieta
 - Atividade física
 - Redução do stress
 - Redução dos gatilhos
 - Métodos Comportamentais
 - Medicamentos
 - Suporte psíquico
 - Cirurgia

**7º CURSO DE ATUALIZAÇÃO EM
GINECOLOGIA INFANTO-JUVENIL E
2º CURSO DE ENDOCRINOLOGIA PEDIÁTRICA**
.....
DO HOSPITAL DA CRIANÇA SANTO ANTÔNIO



**SAVE THE DATE
DE 31 DE AGOSTO A
01 DE SETEMBRO
DE 2018**

ANFITEATRO HUGO GERDAU
RUA PROF. ANNES DIAS, 295 – CENTRO



SANTA CASA
DE MISERICÓRDIA
PORTO ALEGRE



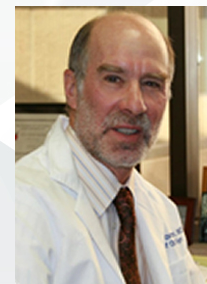
De 2 a 4 de agosto de 2018
Plaza São Rafael | Porto Alegre | RS



Nicolás Crisosto
Santiago / Chile



Joanne Kurtzberg, M.D.
North Carolina / EUA



Alan G. Waxman, M.D.
Albuquerque / EUA

www.sogirgs.org.br/congresso2018

SAVE THE DATE



13 a 16 de novembro de 2019
Porto Alegre RS

Promoção
Realização:

febrasgo
Federação Brasileira das
Associações de Ginecologistas e Obstetras

Apoio:



Organização:



Apoio:



FAÇA SUA INSCRIÇÃO
DURANTE ESTE
EVENTO E TENHA

50%
DE DESCONTO.



Monumento aos açorianos - Porto Alegre

COMPLEXO SANTA CASA DE POA

UFCSPA

Obrigada pela oportunidade!
Liliane Diefenthaeler Herter