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de Pediatria no contexto do 17º Congresso
Nacional de Pediatria, para seu uso
pessoal, tal como submetido pelo autor

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OBESIDADE & DIABETES

Júlia Galhardo





DEFINIÇÕES

www.who.int

OBESIDADE

INSULINA

Resistência

Célula β

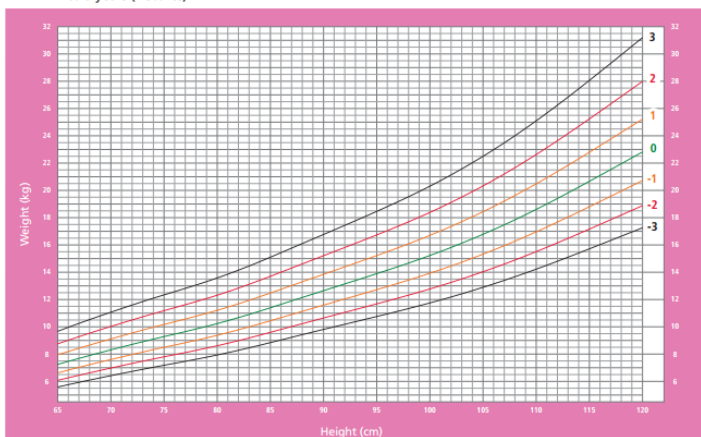
DIABETES

DM2

DM1 Obeso

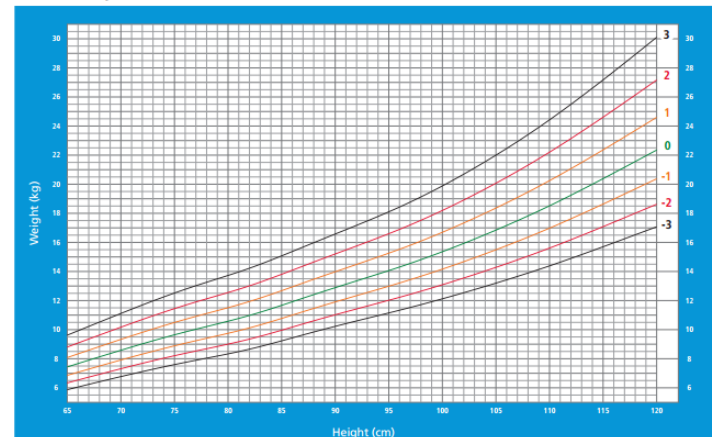
Weight-for-Height GIRLS

2 to 5 years (z-scores)



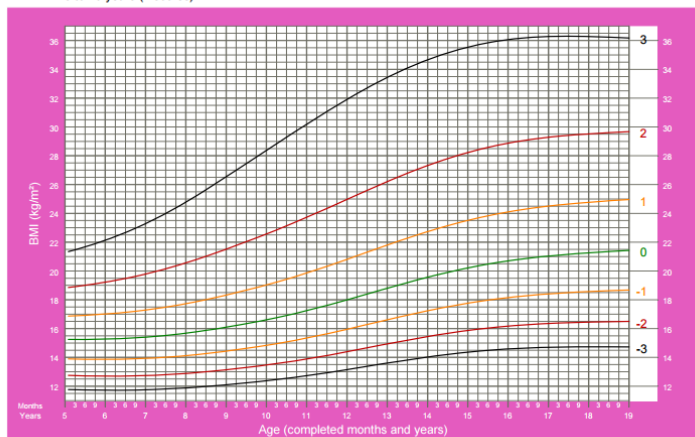
Weight-for-height BOYS

2 to 5 years (z-scores)



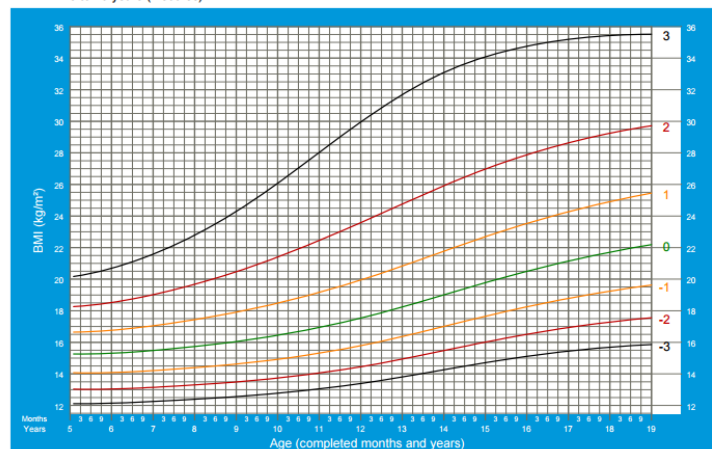
BMI-for-age GIRLS

5 to 19 years (z-scores)



BMI-for-age BOYS

5 to 19 years (z-scores)





DEFINIÇÕES

Antunes A, et al. *Acta Med Port.* 2011; 24: 279-284

OBESIDADE

INSULINA

Resistência

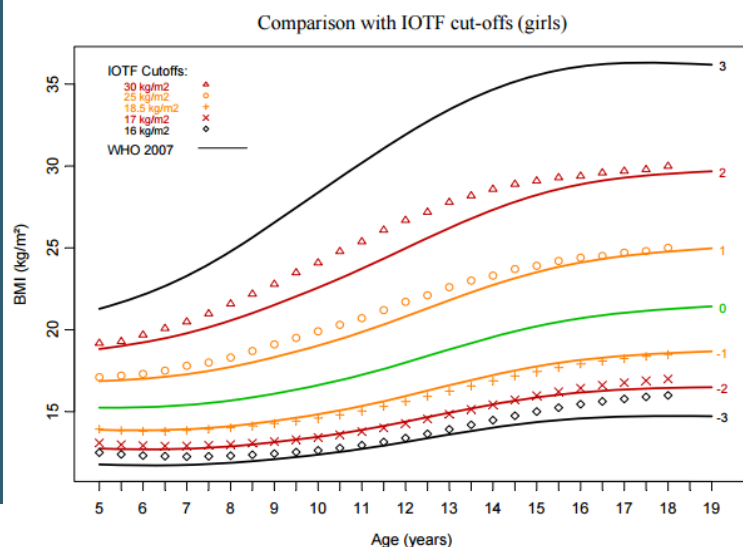
Célula β

DIABETES

DM2

DM1 Obeso

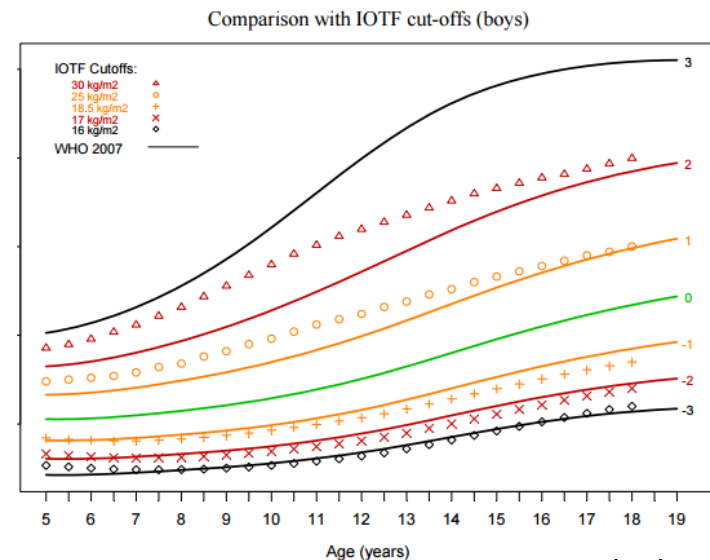
Referência	Definição	Índice utilizado	Pontos de Corte
CDC	Percentil de Índice de Massa Corporal (IMC) para a idade.	Índice de Massa Corporal	Risco de excesso de peso = percentil > 85 e < 95 ; Excesso de Peso = percentil ≥ 95 .
IOTF	Pontos de corte definidos através da intercepção com os pontos de IMC para a classificação de excesso de peso e obesidade em adultos.	Índice de Massa Corporal	Excesso de Peso relativo ao IMC > 25 e < 30 em adultos; Obesidade relativo ao IMC ≥ 30 em adultos.
OMS	Distribuição do z-score de peso para altura, ou seja, relação entre o peso encontrado e o peso ideal para a altura.	Peso e altura	Excesso de Peso = z-score > 1 e < 2 ; Obesidade = z-score ≥ 2



P99

P97

P85





EPIDEMIOLOGIA

www.who.int

OBESIDADE

INSULINA

Resistência

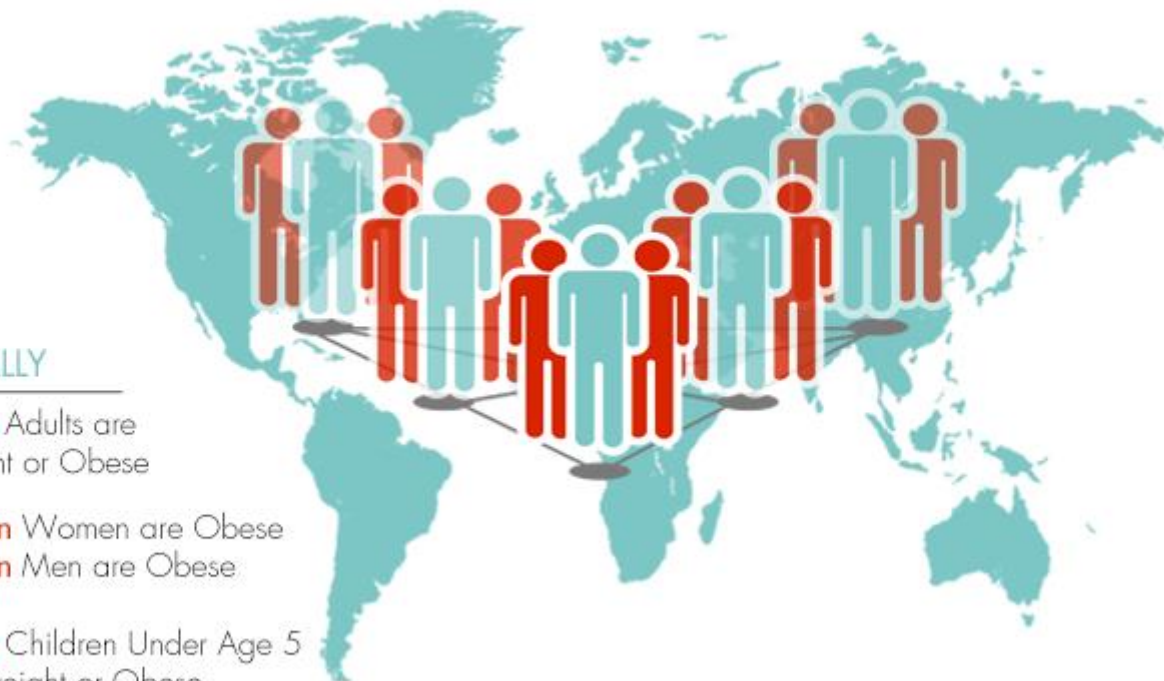
Célula β

DIABETES

DM2

DM1 Obeso

WORLDWIDE OBESITY HAS DOUBLED SINCE 1980



ObesityHelp.com Data Source: World Health Organization (WHO)



2 OUT OF 3 ADULTS ARE
OVERWEIGHT or OBESE



1 OUT OF 3 KIDS ARE
OVERWEIGHT or OBESE





EPIDEMIOLOGIA

www.worldobesity.org



OBESIDADE

INSULINA

Resistência

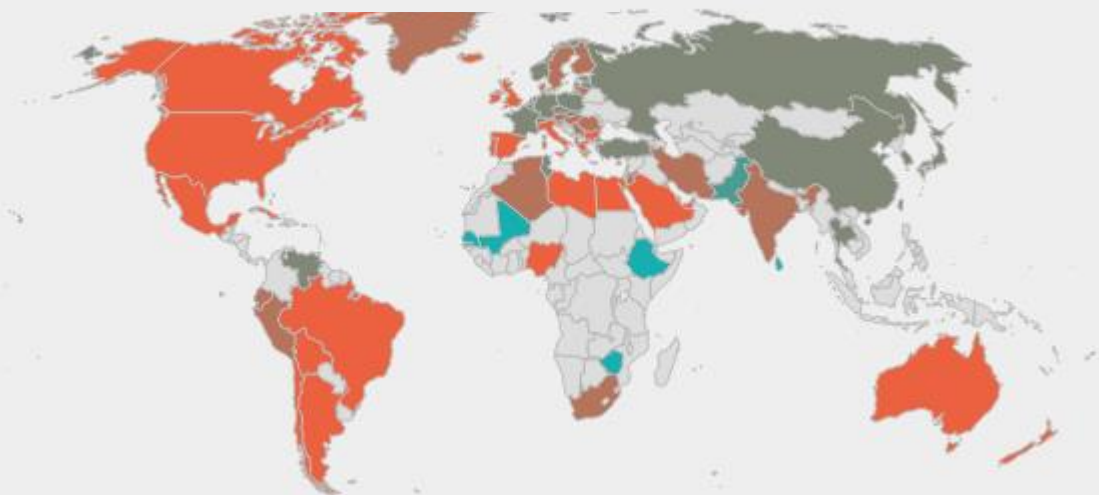
Célula β

DIABETES

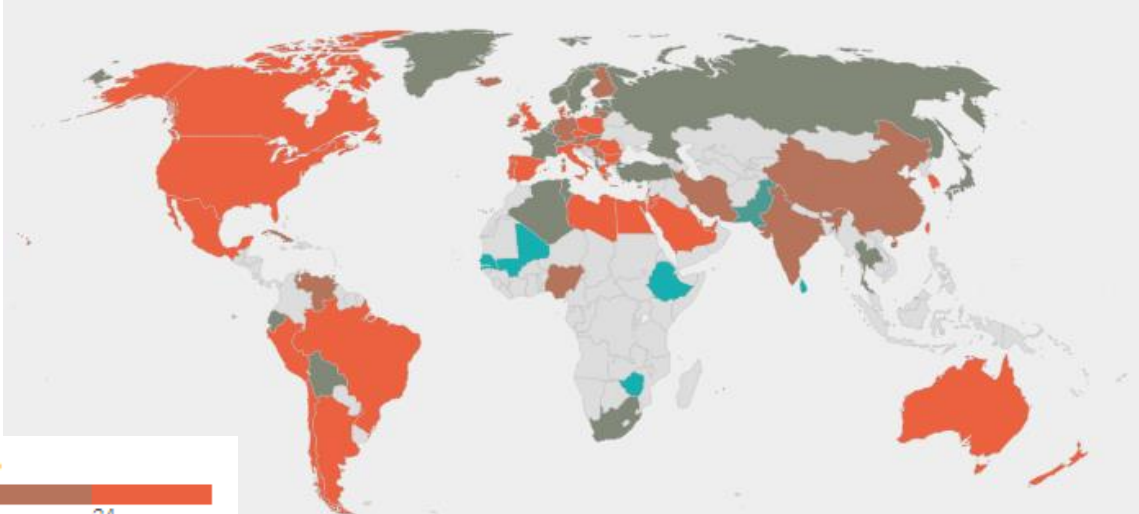
DM2

DM1 Obeso

Obesity prevalence worldwide - Girls



Obesity prevalence worldwide - Boys



Percentage of children with obesity



OBESIDADE

INSULINA

Resistência

Célula β

DIABETES

DM2

DM1 Obeso



Figura 2: Estado nutricional em 2008, 2010 e 2013 de acordo com o critério de classificação da OMS.

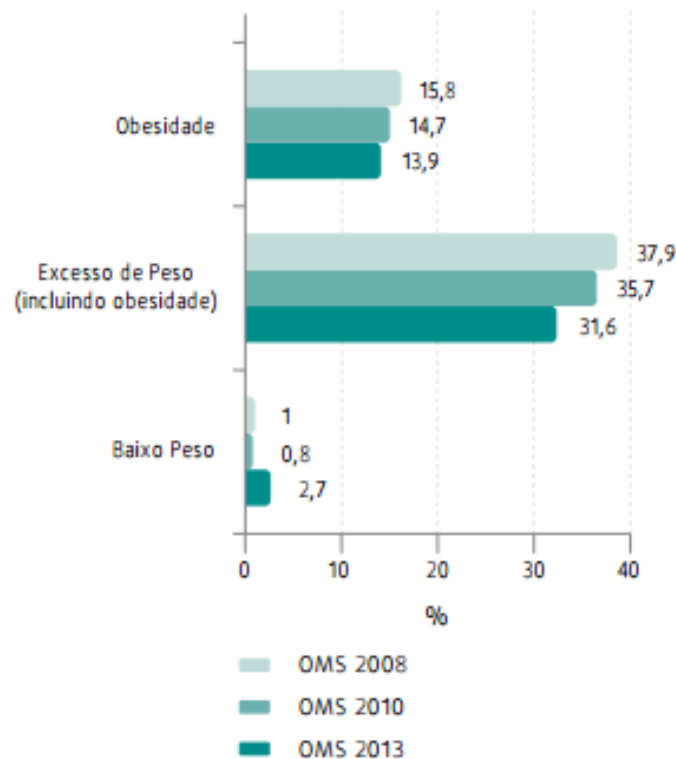
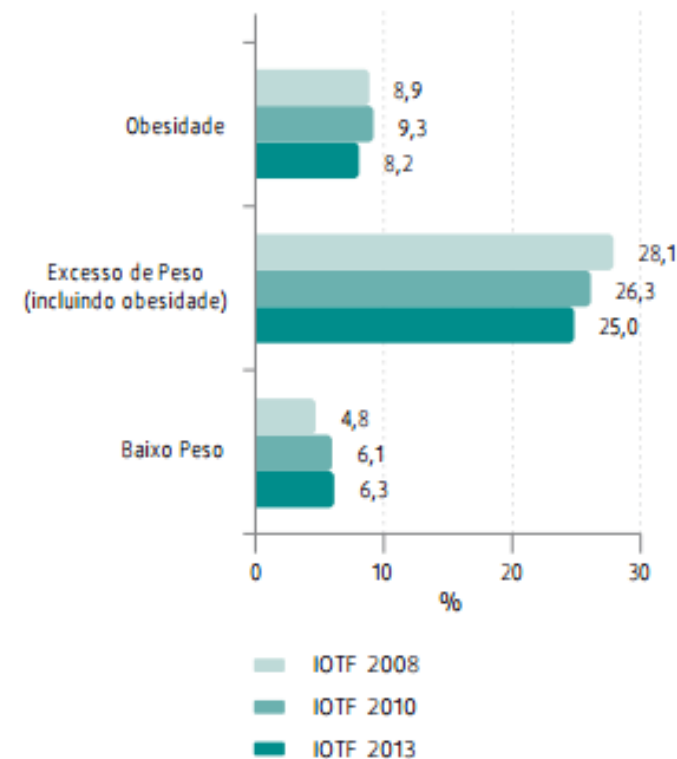


Figura 3: Estado nutricional em 2008, 2010 e 2013 de acordo com o critério de classificação da IOTF.





ETIOLOGIA

Davidson K, et al. *Obes Rev.* 2001; 2: 59-71

OBESIDADE

INSULINA

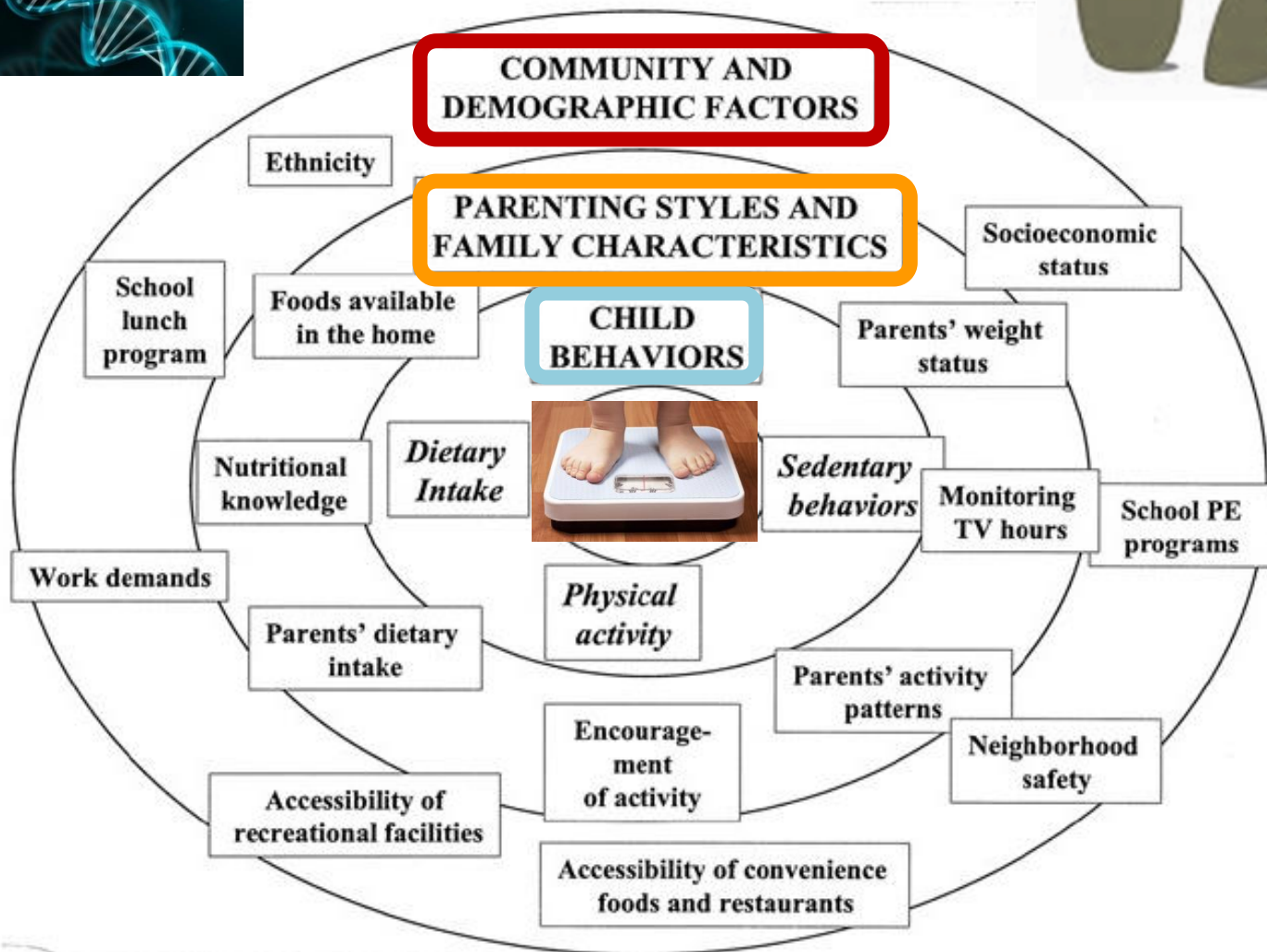
Resistência

Célula β

DIABETES

DM2

DM1 Obeso





COMPLICAÇÕES

Siemaszkiewicz L. *Lancet*. 2005. 5: 260

OBESIDADE

INSULINA

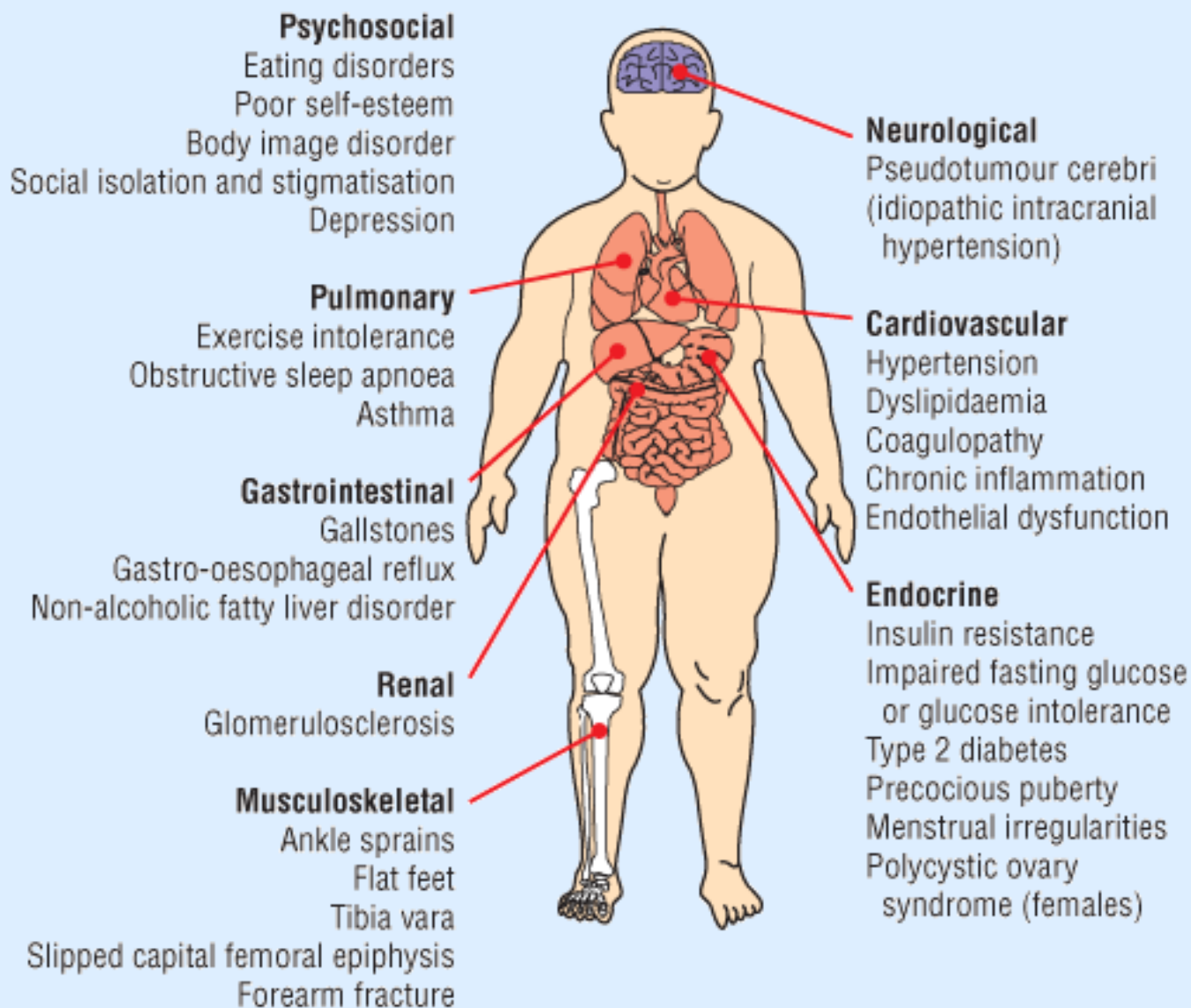
Resistência

Célula β

DIABETES

DM2

DM1 Obeso





SÍNDROME METABÓLICA

www.idf.org

OBESIDADE

INSULINA

Resistência

Célula β

DIABETES

DM2

DM1 Obeso

Consenso da IDF para a Criança e o Adolescente

Age group (years)	Obesity* (WC)	Triglycerides	HDL-C	Blood pressure	Glucose (mmol/L) or known T2DM
6–<10	$\geq 90^{\text{th}}$ percentile	Metabolic syndrome cannot be diagnosed, but further measurements should be made if there is a family history of metabolic syndrome, T2DM, dyslipidemia, cardiovascular disease, hypertension and/or obesity.			
10–<16 Metabolic syndrome	$\geq 90^{\text{th}}$ percentile or adult cut-off if lower	≥ 1.7 mmol/L (≥ 150 mg/dL)	< 1.03 mmol/L (< 40 mg/dL)	Systolic ≥ 130 / diastolic ≥ 85 mm Hg	≥ 5.6 mmol/L (100 mg/dL) (If ≥ 5.6 mmol/L [or known T2DM] recommend an OGTT)
16+ Metabolic syndrome	Use existing IDF criteria for adults, ie: Central obesity (defined as waist circumference ≥ 94 cm for Europid men and ≥ 80 cm for Europid women, with ethnicity specific values for other groups*) plus any two of the following four factors: • raised triglycerides: ≥ 1.7mmol/L • reduced HDL-cholesterol: < 1.03mmol/L (< 40 mg/dL) in males and < 1.29mmol/L (< 50 mg/dL) in females, or specific treatment for these lipid abnormalities • raised blood pressure: systolic Bp ≥ 130 or diastolic Bp ≥ 85mm Hg, or treatment of previously diagnosed hypertension • impaired fasting glycemia (IFG): fasting plasma glucose (FPG) ≥ 5.6 mmol/L (≥ 100 mg/dL), or previously diagnosed type 2 diabetes				





FENÓTIPOS

Heianza Y et al. *JCEM*. 2014; 99: 2952-60

OBESIDADE

INSULINA

Resistência

Célula β

DIABETES

DM2

DM1 Obeso

IMC adequado

IMC > P85

Normoglicemia

Normolipidemia



Fat - Fit

Hiperglicemia

Dislipidemia



Slim - Sick





FUNÇÃO ANABÓLICA

Bunner AE et al. *World J Diab.* 2014; 5(2): 146-152

OBESIDADE

INSULINA

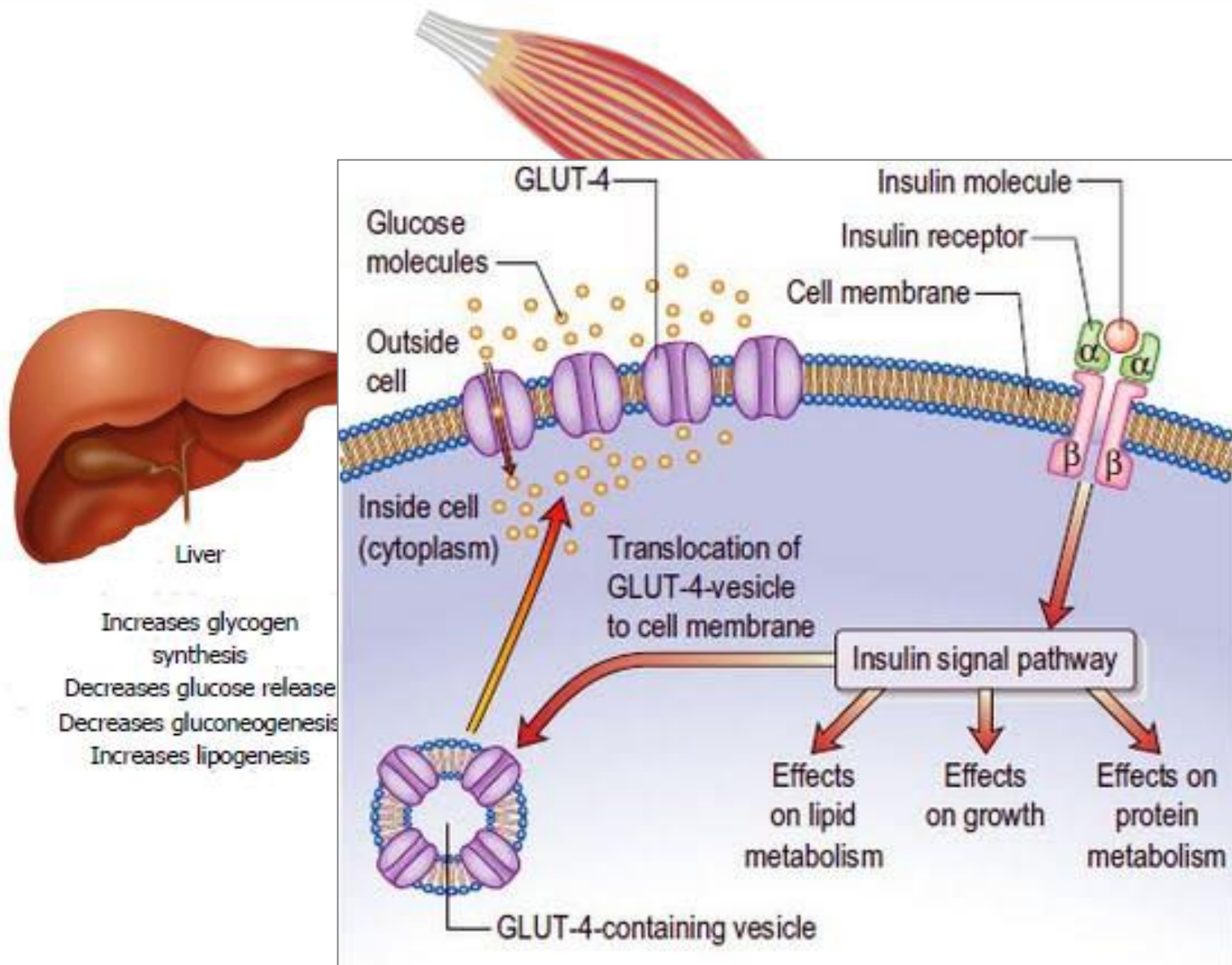
Resistência

Célula β

DIABETES

DM2

DM1 Obeso





GORDURA VISCERAL

Stefen N et al. *Lancet Diab Endo*. 2013; 1(2): 152-62

OBESIDADE

INSULINA

Resistência

Célula β

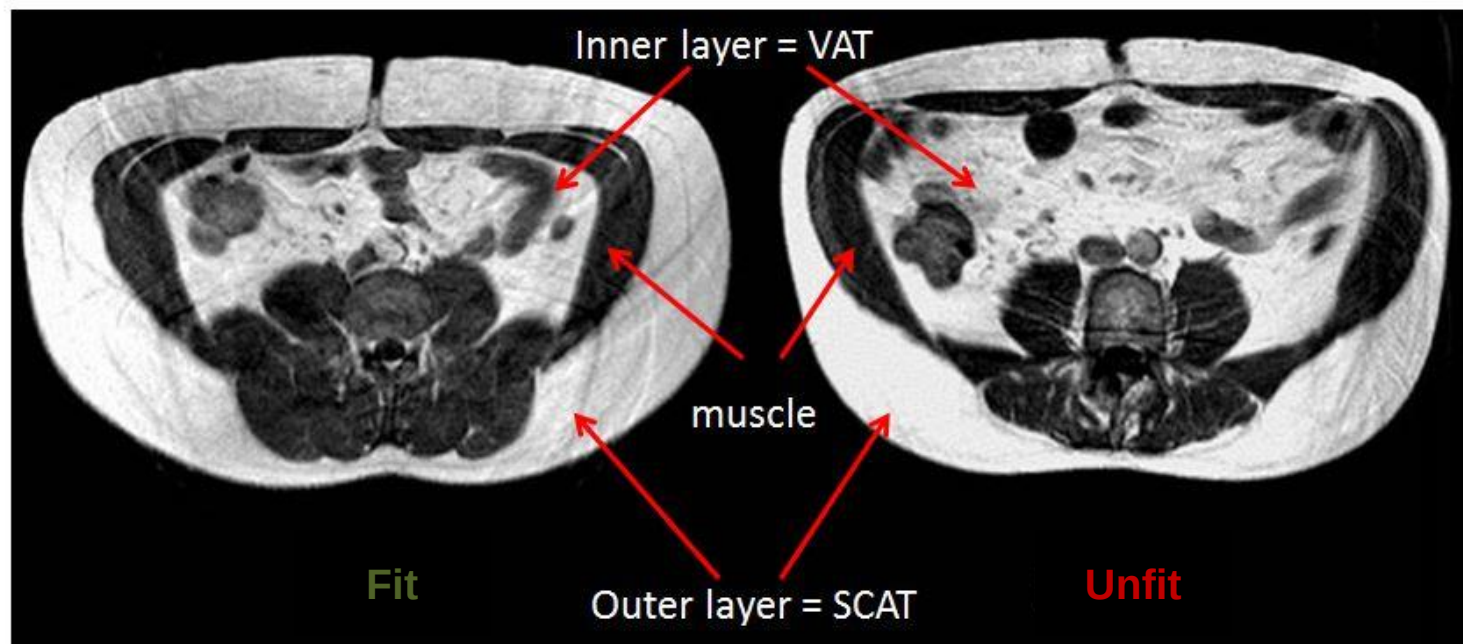
DIABETES

DM2

DM1 Obeso

Sensível

Resistente





TECIDO ADIPOSEO

Lackey DE, et al. *Nature Rev Endo.* 2016; 12: 15-28

OBESIDADE

INSULINA

Resistência

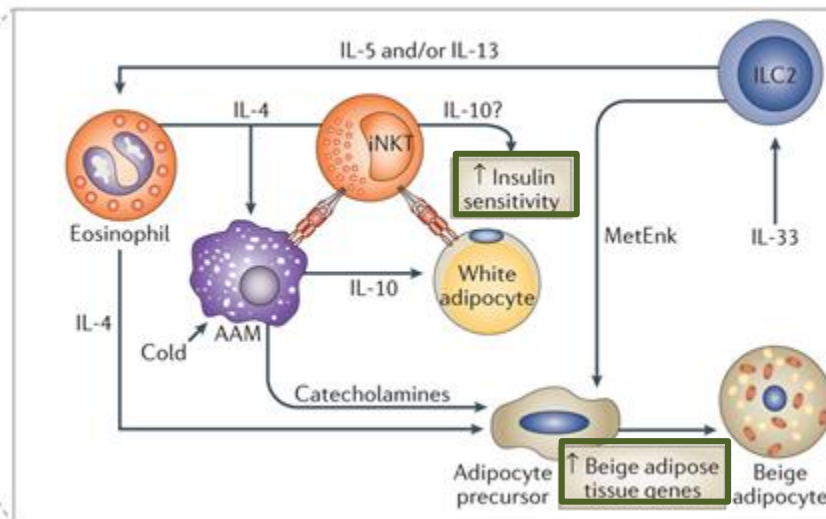
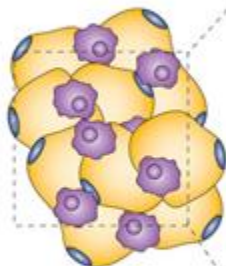
Célula β

DIABETES

DM2

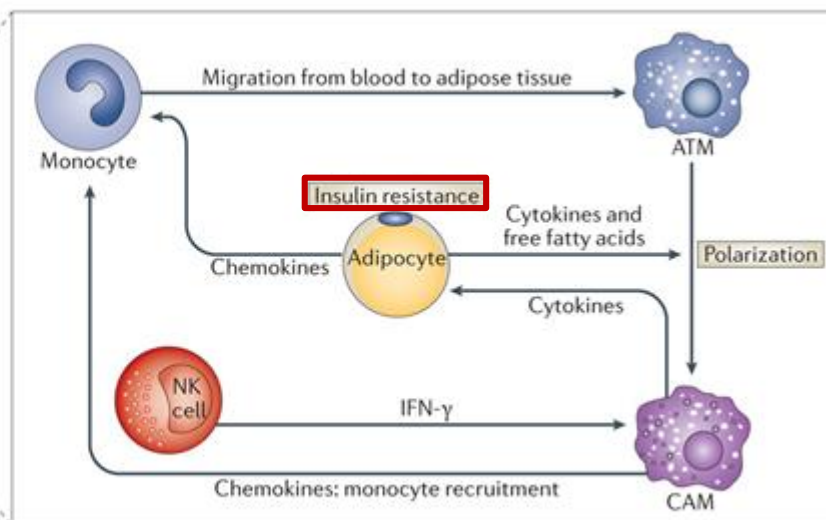
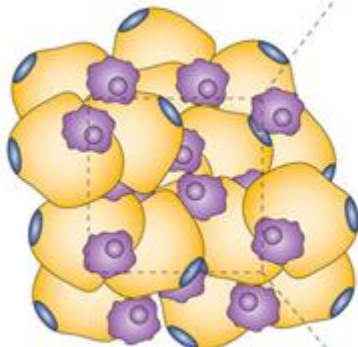
DM1 Obeso

Sensível



Frio
Exercício
Catecolaminas
FGF-21
Irisina

Resistente

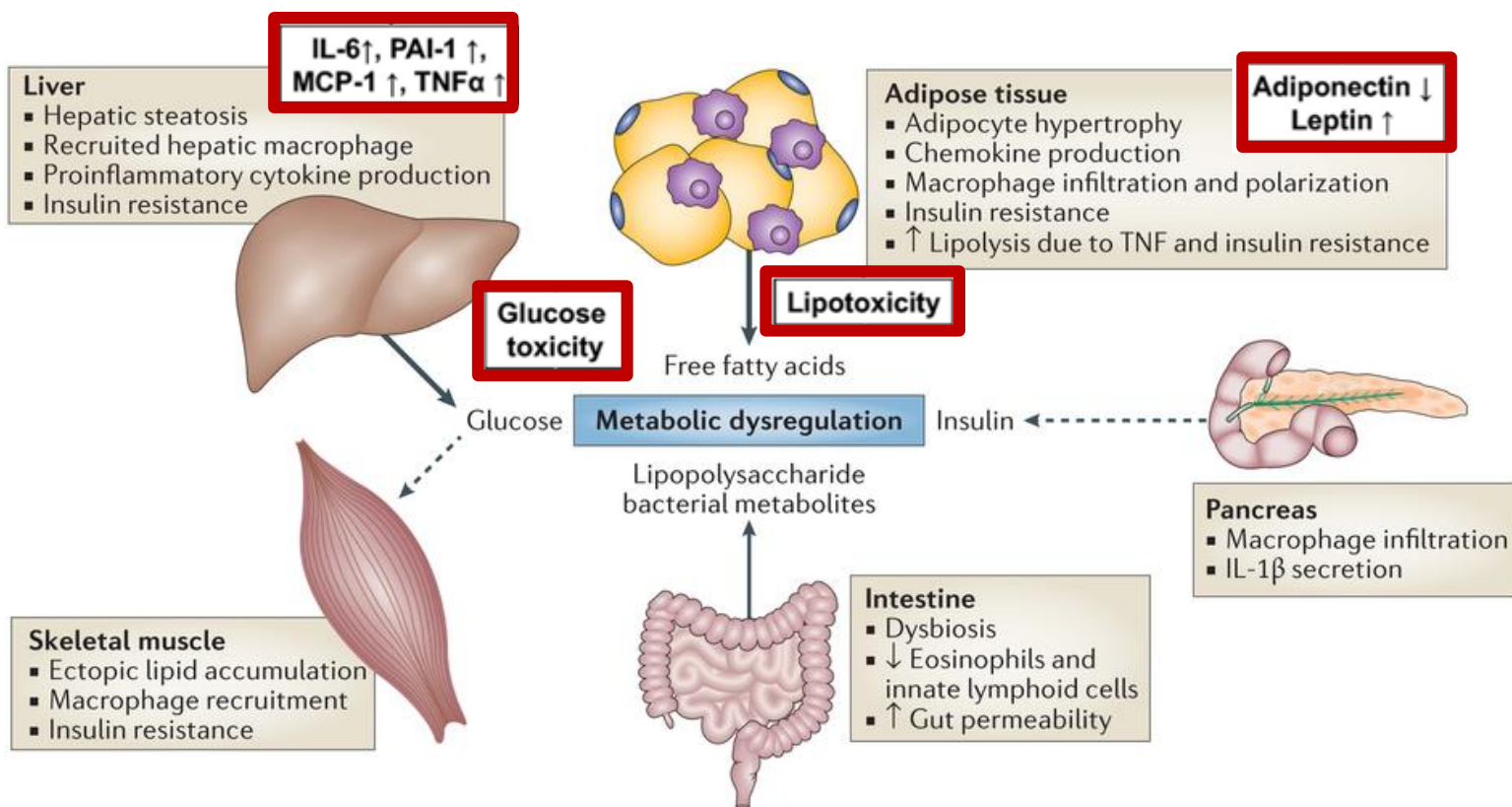


Hipóxia
Apoptose
↑ FFA
Inflamação Sist
↑ ROS

INSULINORRESISTÊNCIA

Lackey DE, et al. *Nature Rev Endo*. 2016; 12: 15-28

Inflamação Crônica e Acumulação de Gordura Ectópica



CÉLULAS - ALVO

Serra D, et al. *Antiox Redox Signal.* 2013; 19(3): 269-84

OBESIDADE

INSULINA

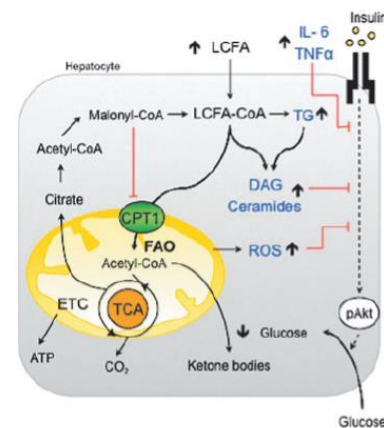
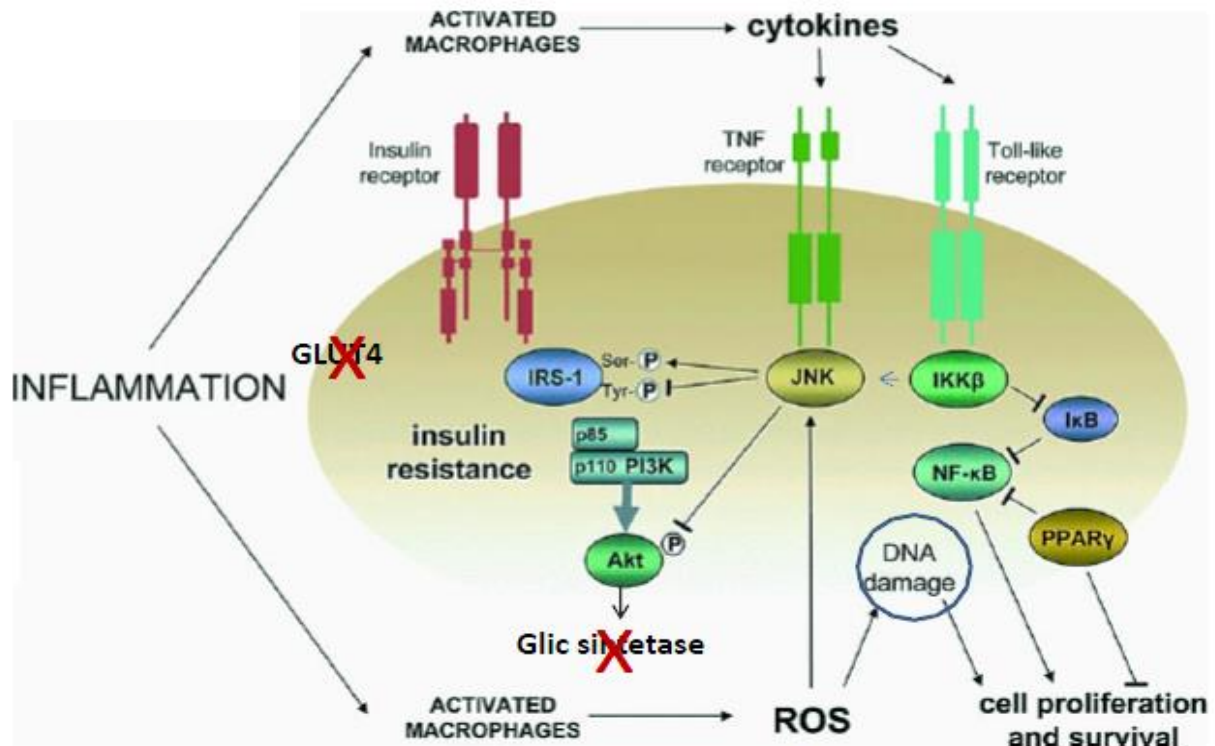
Resistência

Célula β

DIABETES

DM2

DM1 Obeso



SECREÇÃO E SENSIBILIDADE

Arslanian SA et al. *Horm Res.* 2005; 64(3): 16-24

Bacha F et al. *Diabetes Care.* 2010; 33(10): 2255-31

OBESIDADE

INSULINA

Resistência

Célula β

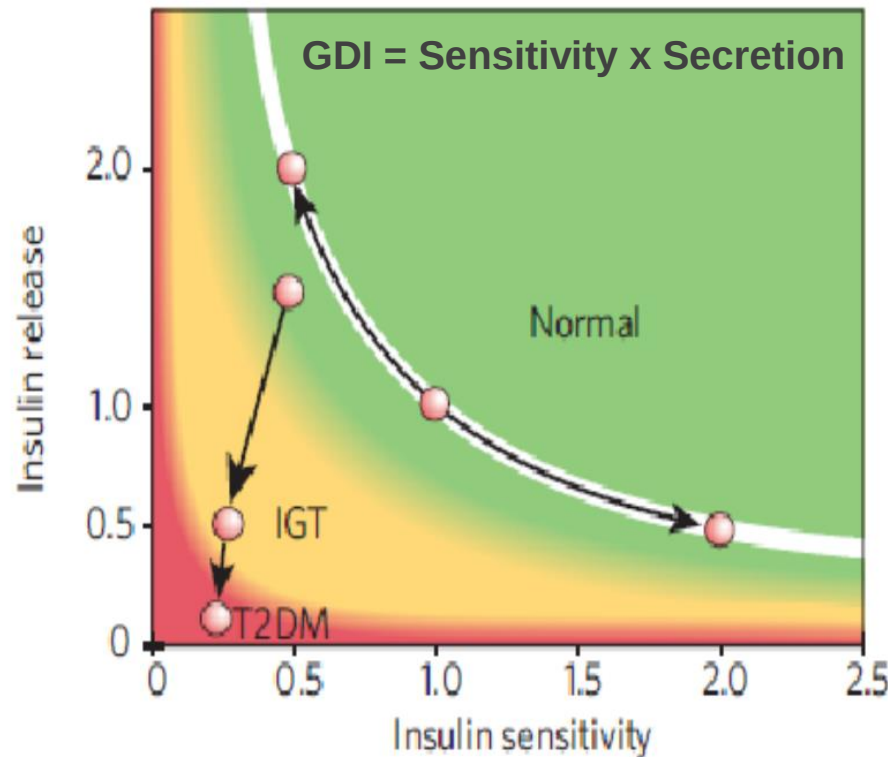
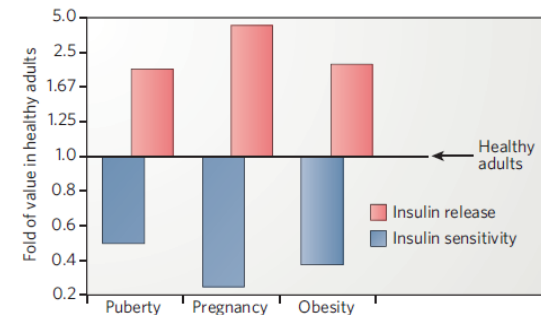
DIABETES

DM2

DM1 Obeso

Clamp
Hiperglicémico

Gold-standard



Clamp
Hiperinsulinémico -
Euglicémico





SECREÇÃO E SENSIBILIDADE

Kurtoglu S et al. *J Clin Res Ped Endo*. 2010; 2(3): 100-6

OBESIDADE

INSULINA

Resistência

Célula β

DIABETES

DM2

DM1 Obeso

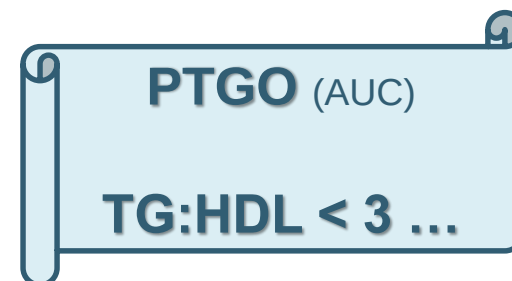
Homeostasis Model Assessment

HOMA-IR	$(\text{Glucose J} \times \text{Insulina J}) / 22.5$	$(\text{Glucose J} \times \text{Insulina J}) / 405$
HOMA- β	$(20 \times \text{Insulina J}) / (\text{Glucose J} - 3.5)$	$(360 \times \text{Insulina J}) / (\text{Glucose J} - 63)$
	Glucose em mmol/L	Glucose em mg/dL

HOMA-IR Normal

- Adulto: < 2.5
- Adulto Hispânico: < 3.8
- Puberdade: < 3.1

- Sem standards para a criança
- Sem standards pubertários de acordo com o sexo e a etnia





PUBERDADE

Cree-Green M, et al. *Curr Diab Rep.* 2013; 13(1): 81-88

OBESIDADE

INSULINA

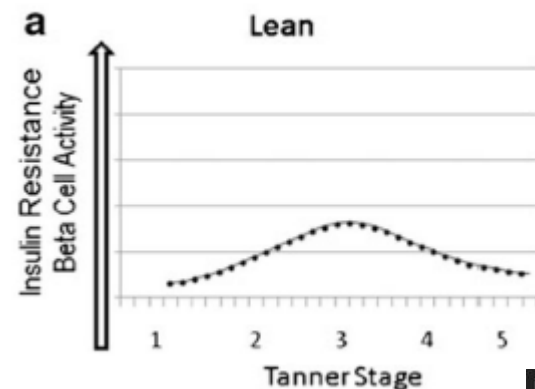
Resistência

Célula β

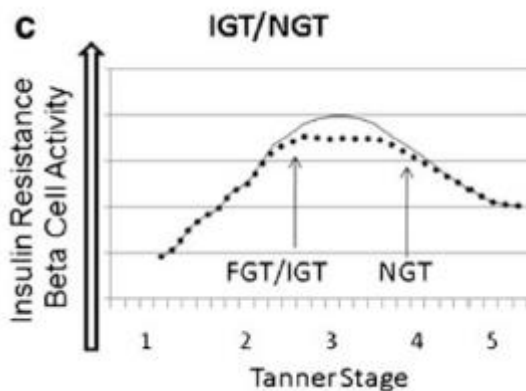
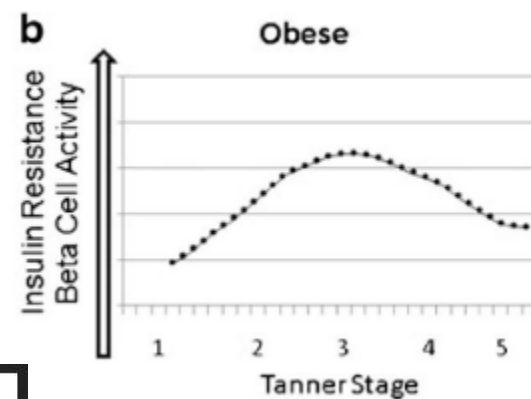
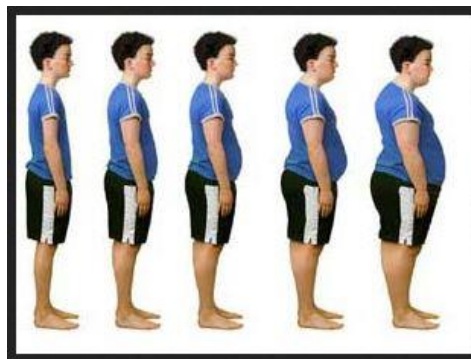
DIABETES

DM2

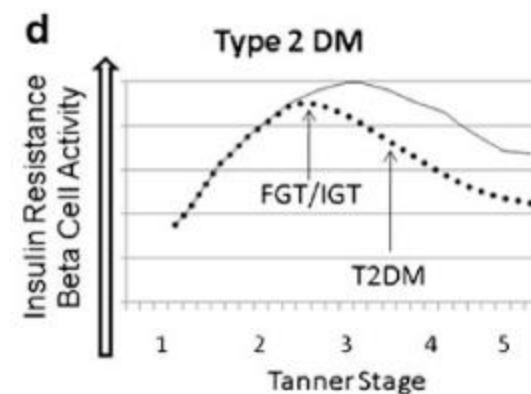
DM1 Obeso



↑ 25-50% IR



Hispano-Americanos
Afro-Americanos
Asiáticos





PROGRAMAÇÃO DA CÉLULA β

Cerf ME. *Ped Diab.* 2015; 16: 71-78

OBESIDADE

INSULINA

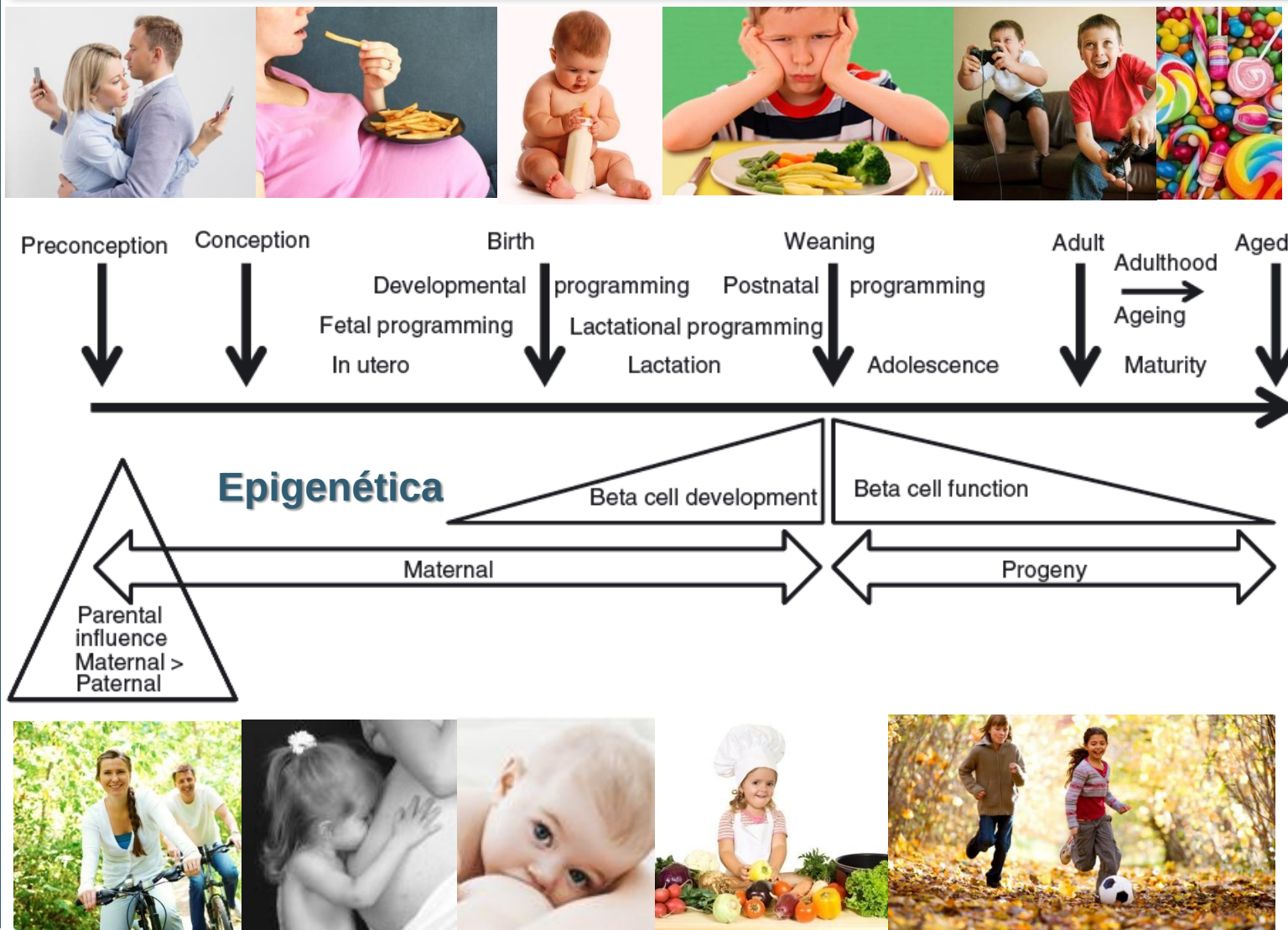
Resistência

Célula β

DIABETES

DM2

DM1 Obeso





(DES)ADAPTAÇÃO

Cerf ME. *Ped Diab*. 2015; 16: 71-78

Giannini C, et al. *Curr Diab Rep*. 2013; 13(1): 89-95

OBESIDADE

INSULINA

Resistência

Célula β

DIABETES

DM2

DM1 Obeso



HIGH FAT PROGRAMMING

Hyperglycemia

Acute

Beta cell compensation

Hyperplasia
Hypertrophy
Increased proliferation
Recruitment of progenitors
Hyperinsulinemia

Chronic

Chronic

Insulin resistance

Impaired systemic glucose clearance and uptake in glucose recipient organs (e.g., skeletal muscle liver and adipose tissue)

↑ ROS

Inflamação

Disfunção RE

Beta cell exhaustion

Hypoplasia
Hypotrophy
Reduced proliferation
Dedifferentiation

Beta cell death

Beta cell dysfunction

Reduced insulin synthesis
Decreased insulin signaling
Impaired insulin secretion

Type 2 diabetes





RASTREIO

ADA. *Diab Care*. 2016; 39 (1): S13-S22

ISPAD. *Ped Diab*. 2014; 15 (Suppl 20): 26-46

OBESIDADE

INSULINA

Resistência

Célula β

DIABETES

DM2

DM1 Obeso

População de Risco

Table 2.4—Testing for type 2 diabetes or prediabetes in asymptomatic children*

Criteria

- **Overweight** (BMI >85th percentile for age and sex, weight for height >85th percentile, or weight >120% of ideal for height)

Plus any two of the following risk factors:

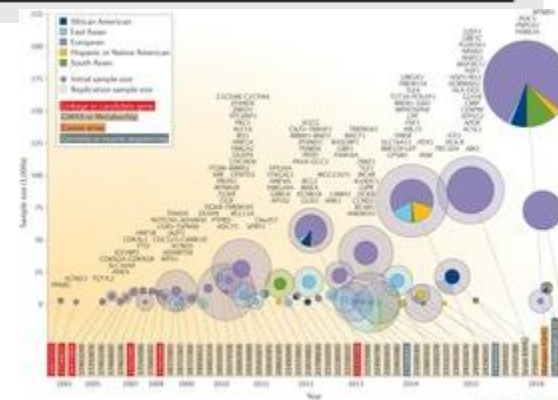
- Family history of type 2 diabetes in first- or second-degree relative
- Race/ethnicity (Native American, African American, Latino, Asian American, Pacific Islander)
- Signs of insulin resistance or conditions associated with insulin resistance (acanthosis nigricans, hypertension, dyslipidemia, polycystic ovary syndrome, or small-for-gestational-age birth weight)
- Maternal history of diabetes or GDM during the child's gestation

Age of initiation: age 10 years or at onset of puberty, if puberty occurs at a younger age

Frequency: every 3 years

Japão (60-80%)

- glicosúria a todos os adolescentes



Florez J et al. *Nature Rev Gen*. 2016; 17 (1): 535-49





DIAGNÓSTICO

ADA. *Diab Care*. 2016; 39 (1): S13-S22

ISPAD. *Ped Diab*. 2014; 15 (Suppl 20): 26-46

OBESIDADE

INSULINA

Resistência

Célula β

DIABETES

DM2

DM1 Obeso

Table 2.3—Categories of increased risk for diabetes (prediabetes)*

FPG 100 mg/dL (5.6 mmol/L) to 125 mg/dL (6.9 mmol/L) (IFG)

OR

2-h PG in the 75-g OGTT 140 mg/dL (7.8 mmol/L) to 199 mg/dL (11.0 mmol/L) (IGT)

OR

A1C 5.7–6.4% (39–46 mmol/mol)

?

Table 2.1—Criteria for the diagnosis of diabetes

FPG ≥ 126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 h.*

OR

2-h PG ≥ 200 mg/dL (11.1 mmol/L) during an OGTT. The test should be performed as described by the WHO, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.*

OR

A1C $\geq 6.5\%$ (48 mmol/mol). The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.*

OR

In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥ 200 mg/dL (11.1 mmol/L).

*In the absence of unequivocal hyperglycemia, results should be confirmed by repeat testing.

?





DIAGNÓSTICO

ISPAD. *Ped Diab.* 2014; 15 (Suppl 20): 4-17

OBESIDADE

INSULINA

Resistência

Célula β

DIABETES

DM2

DM1 Obeso

Table 3. Clinical characteristics of type 1, type 2 and monogenic diabetes in children and adolescents

Characteristic	Type 1	LADY (1.5)?	Type 2	Monogenic
Genetics	Polygenic		Polygenic	Monogenic
Age of onset	6 months to young adulthood		Usually <u>pubertal (or later)</u>	<u>Often postpubertal</u> except GCK and NDM
Clinical presentation	Most often acute, rapid		Variable; from slow, mild (<u>often insidious</u>) to severe	Variable (may be incidental in GCK)
Associations				
Autoimmunity	Yes DM1b ?		No 10-20% Atc ?	No
Ketosis	Common		Uncommon	Common in NDM, rare in other forms
Obesity	<u>Population frequency</u>		<u>Increased frequency</u>	<u>Population frequency</u>
Acanthosis nigricans	<u>No</u>		<u>Yes</u>	<u>No</u>
Frequency (% of all diabetes in young people)	Usually >90%		Most countries <10% (Japan 60–80%)	1–4%
Parent with diabetes	2–4%		<u>80%</u>	<u>90%</u>

The Time Is Right for a New Classification System for Diabetes: Rationale and Implications of the β -Cell–Centric Classification Schema

Stanley S. Schwartz¹†, Solomon Epstein², Barbara E. Corkey³, Struan F.A. Grant⁴, James R. Gavin III⁵ and Richard B. Aguilar⁶



Diabetes Care. 2016; 39 (2): 179-86





ABORDAGEM

ISPAD. *Ped Diab.* 2014; 15 (Suppl 20): 26-46

OBESIDADE

INSULINA

Resistência

Célula β

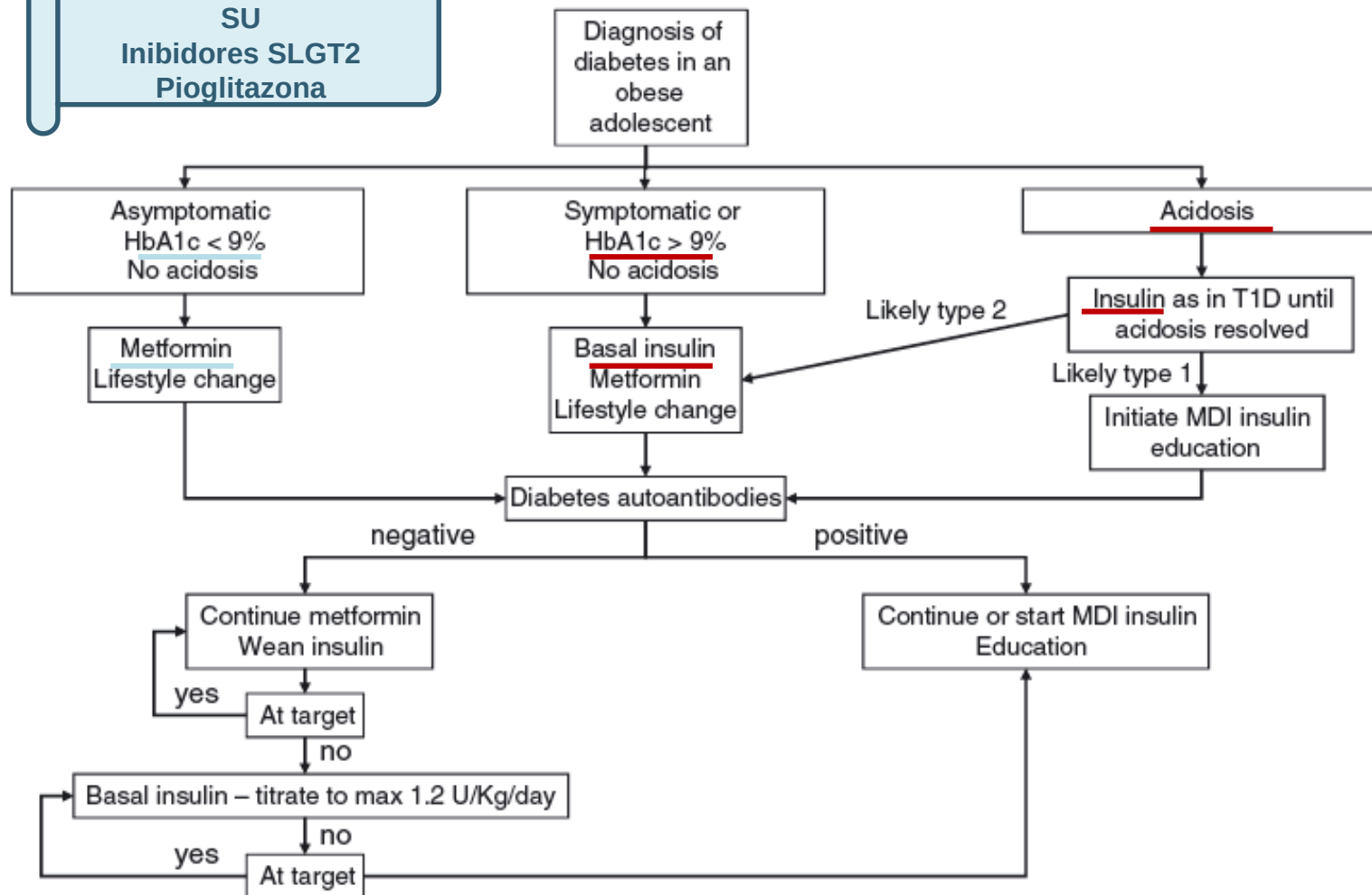
DIABETES

DM2

DM1 Obeso

TODAY

GLP-1
Inibidores DPP-IV
SU
Inibidores SLGT2
Pioglitazona





COMORBILIDADES

ISPAD. *Ped Diab.* 2014; 15 (Suppl 20): 26-46

ISPAD. *Ped Diab.* 2014; 15 (Suppl 20): 257-69

OBESIDADE

INSULINA

Resistência

Célula β

DIABETES

DM2

DM1 Obeso

• Albuminúria

• Retinopatia

• Neuropatia

• Dislipidemia

• EHNA

• SOPQ

• SAOS

• HTA

• Tabagismo

**Diagnóstico
Anualmente**

Regularmente

Sempre

Parameter	Target level
HbA1c (DCCT standard)	<7.5% (<58 mmol/mol) without severe hypoglycemia
LDL cholesterol	<2.6 mmol/L (100 mg/dL)
HDL cholesterol	>1.1 mmol/L (40 mg/dL)
Triglycerides	<1.7 mmol/L (150 mg/dL)
Blood pressure	<90th percentile by age, sex, and height <130/80 for adolescents
ACR	<2.5–25 mg/mmol in males <3.5–25-mg/mmol in females
BMI	<95th percentile (non-obese)
Smoking	None
Physical activity	>1 h of moderate physical activity daily
Sedentary activities	<2 h daily
Healthy diet	Caloric intake appropriate for age and normal growth. Fat <30% of caloric intake, saturated fat <10% of caloric intake. Fiber intake 25–35 g daily. Increased intake of fresh fruit and vegetables.



>> Risco de morte por DCV relativamente ao adulto DM2 e jovem DM1



DIABETES DUPLA

Baskaran C, et al. *Ped Diab.* 2015; 16: 263-70

Schechter R, et al. *Curr Diab Rep.* 2015; 15: 77-89

OBESIDADE

INSULINA

Resistência

Célula β

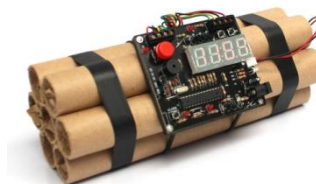
DIABETES

DM2

DM1 Obeso

Sexo Feminino
Puberdade

↑ **PESO**



↑ **DDT Insulina**



↑ **IR**

Metformina

Alimentação

Exercício

GLP-1
Inibidores DPP-IV
Inibidores SGLT2





unidos pela diabetes

14 de novembro

juliagalhardo@chlc.min-saude.pt