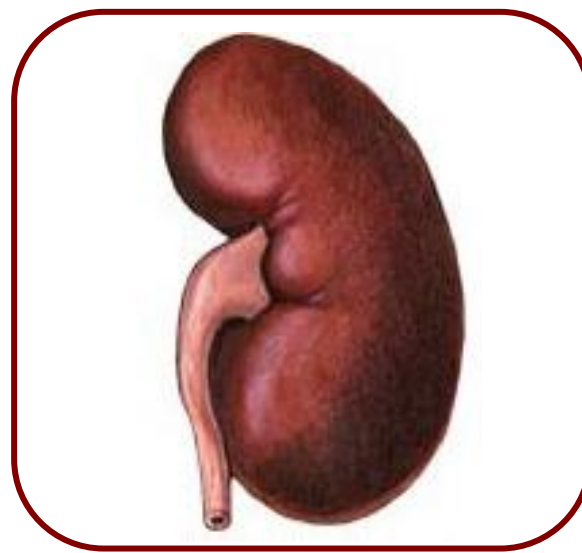


Obrigada por ver esta apresentação
Gostaríamos de recordar-lhe que esta
apresentação é propriedade do autor.

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de Pediatria no contexto do 16º
Congresso Nacional de Pediatria, para
seu uso pessoal, tal como submetido pelo
autor

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ALL THOSE FAT YEARS

CONSEQUÊNCIAS RENAIS DA OBESIDADE

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SÃO JOÃO

16º CONGRESSO NACIONAL DE PEDIATRIA
Albufeira, 23 de Outubro de 2015

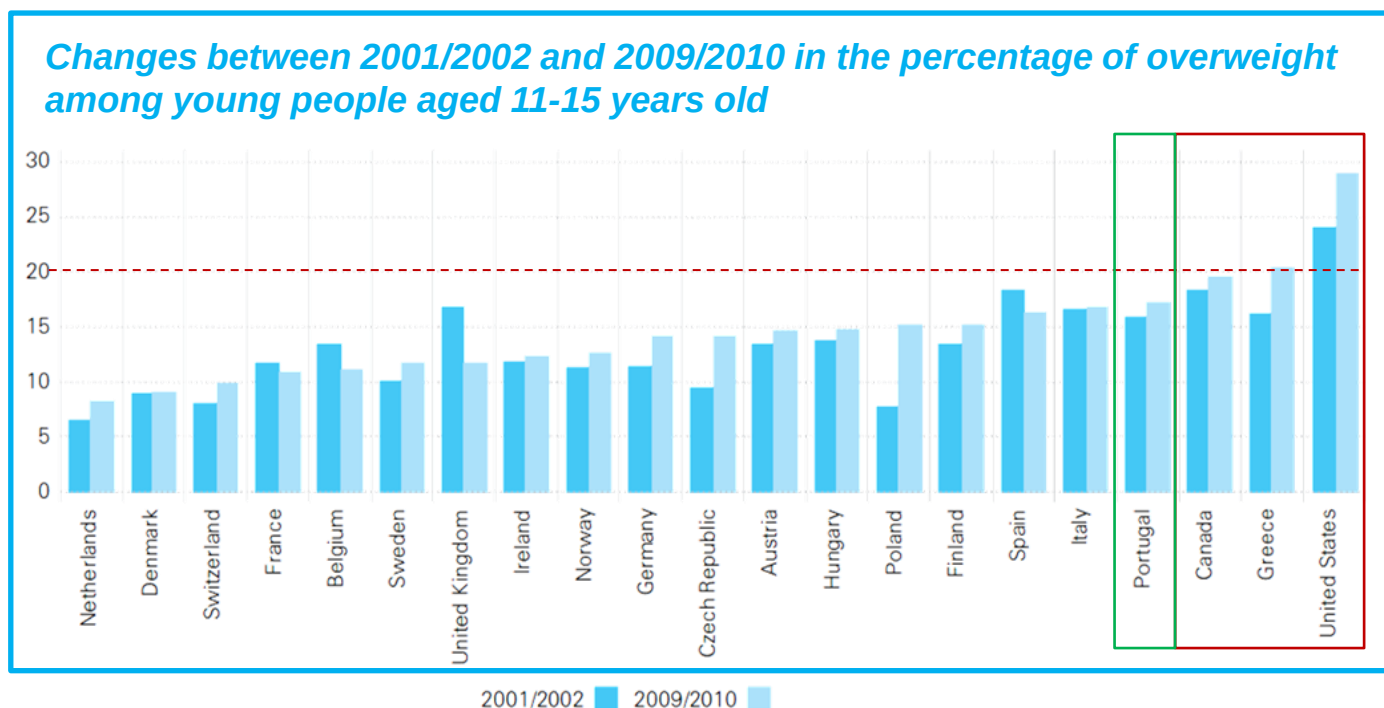
Epidemiologia da obesidade e co-morbilidades

2013
47.1%
1980

PREVALÊNCIA DE EXCESSO DE PESO/OBESIDADE EM CRIANÇAS

Global Burden Disease Study

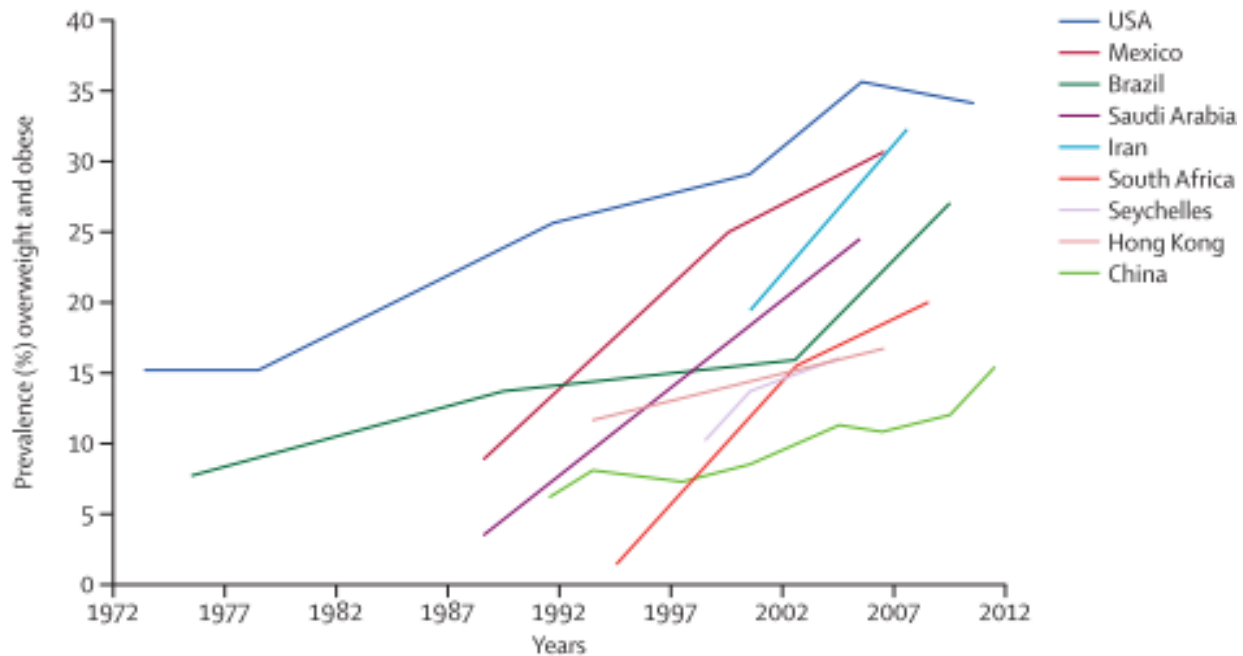
Ng M et al. Lancet 2014;384:766–81.



**Prevalência
≥20%**

Epidemiologia da obesidade e co-morbididades

Prevalence trends for childhood overweight and obesity in the USA and 8 low-income and middle-income countries

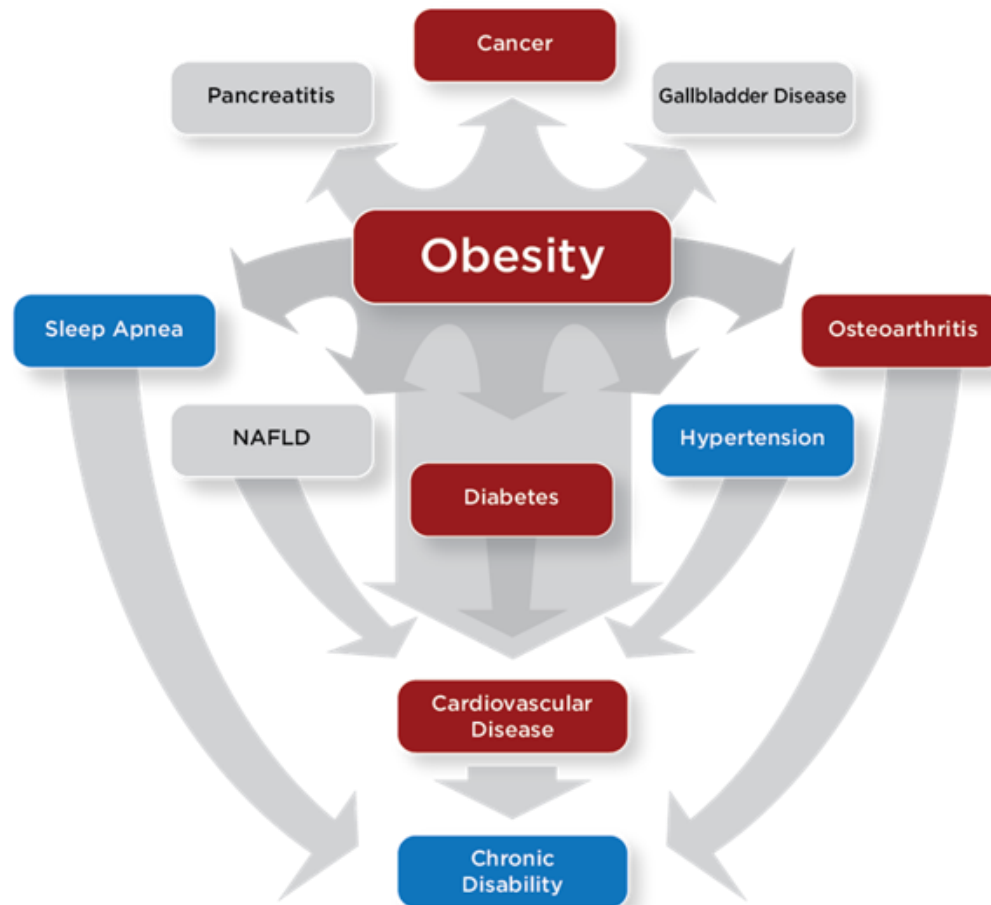


Reproduzido de Lobstein T et al, Lancet 2015.; 385:2510-20.
World Obesity Federation.

Epidemiologia da obesidade e co-morbilidades

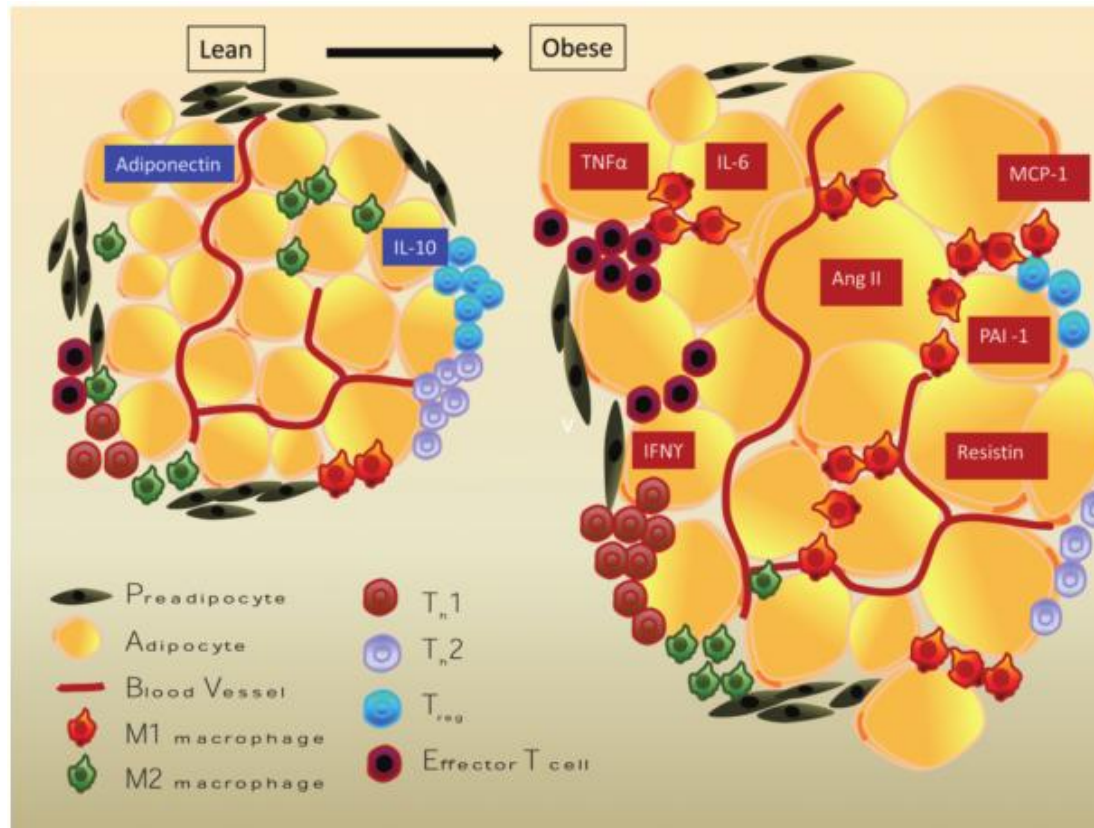
A **obesidade** em idade pediátrica conduz ao desenvolvimento de várias **co-morbilidades cardiovasculares**

Friedemann C et al, BMJ 2012; 345:e4759.



Inflamação, stress oxidativo e dano vascular

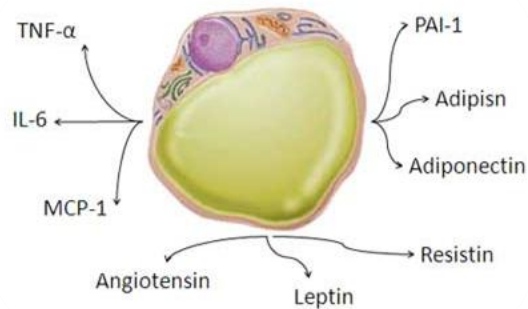
Alterações nas populações imunes e produção de adipocinas do tecido adiposo



Reproduzido de Kalupahana NS et al, *Obes Ver* 2011;13:136–49.

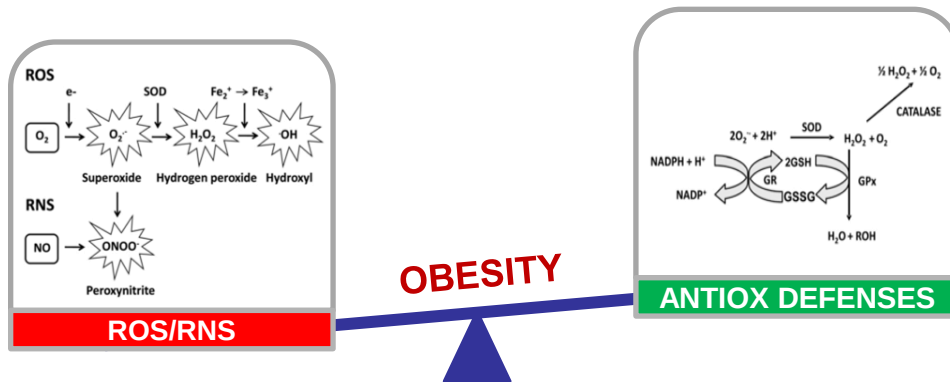
Inflamação, stress oxidativo e dano vascular

A obesidade é um **estado pró-inflamatório e pró-oxidante**



Markers of inflammation and adipokines have been identified to be associated with obesity indexes and CV risk factors in children

Soriano-Guillén L et al, Eur J Endocrinol 2008; 159(1):R1–4.



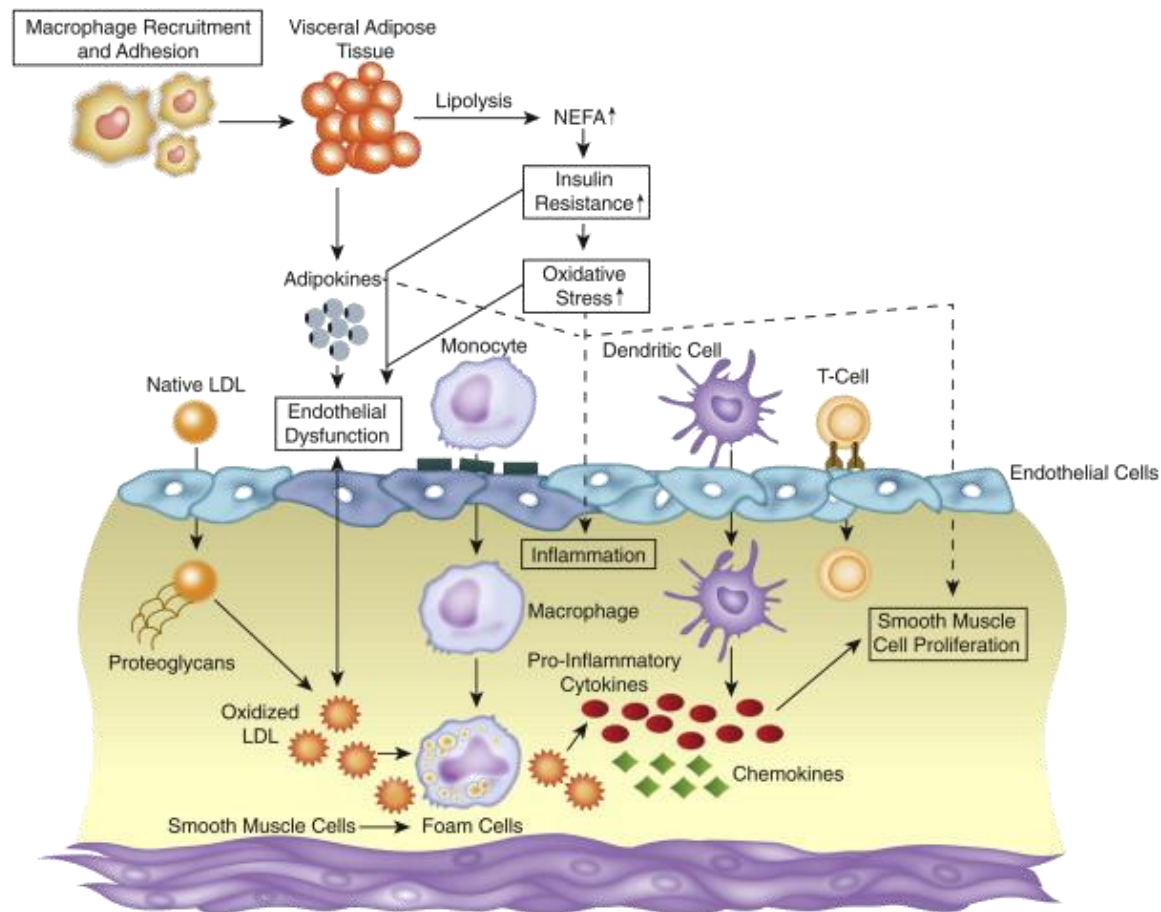
Obese children present higher levels of several parameters of oxidative stress and these parameters are associated with several CV risk factors

Codoner-Franch P et al, Transl Res 2011; 158(6):369–84.

Inflamação, stress oxidativo e dano vascular

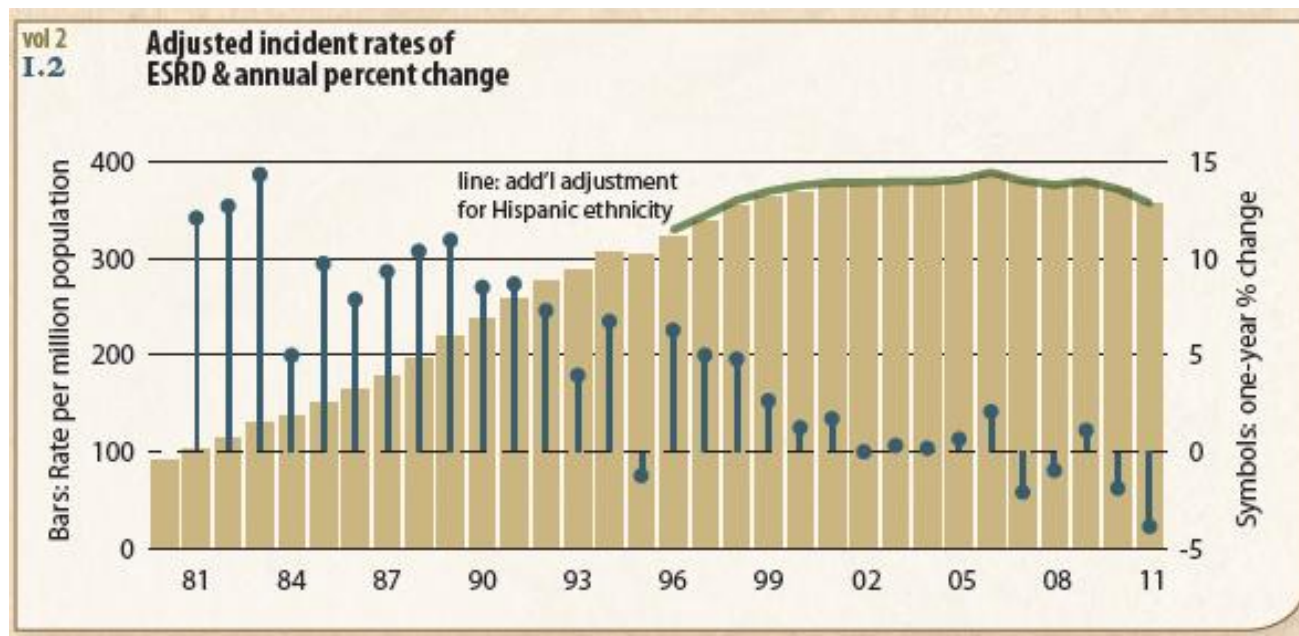
Obesidade induz **disfunção endotelial** e **perda das propriedades fisiológicas** (vasodilatação, fibrinólise e anti-agregação)

Codoner-Franch P et al, Transl Res 2011; 158(6):369–84.



A prevalência de **doença renal crônica terminal** duplicou na última década

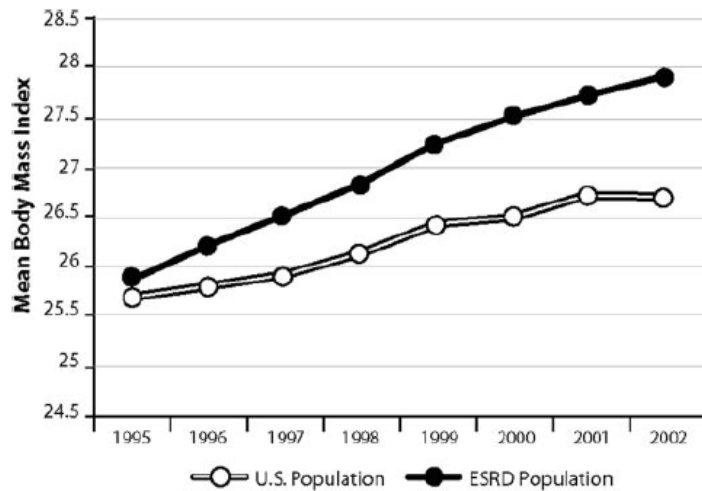
Kalaitzidis RG et al, Int Urol Nephrol 2011; 43(3):771–84.



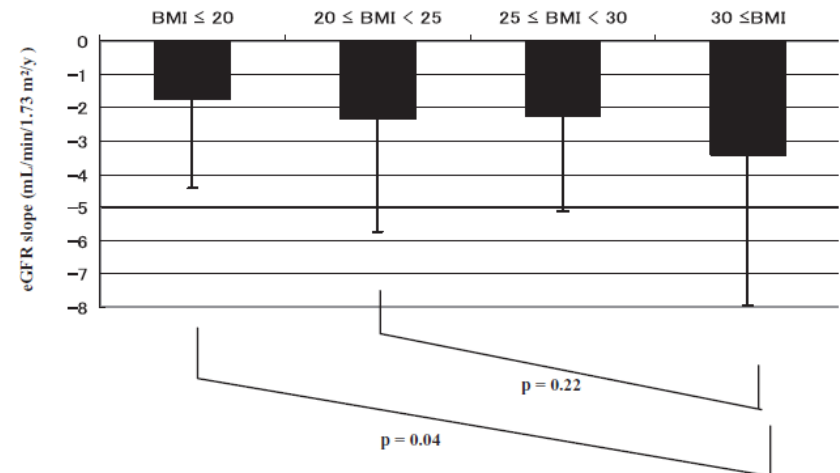
In *Incidence, prevalence, patient characteristics and treatment modalities* - 2013 Atlas of CKD & ESRD from the UNITED STATES RENAL DATA SYSTEM (accessed on <http://www.usrds.org/atlas.aspx>, on 3th Sept 2014)

A obesidade foi identificada como um importante factor de risco para desenvolvimento e progressão de doença renal

Hsu C et al, Ann Intern Med 06; 144(1):21–8.
Wang Y et al, Kidney Int 2008; 73(1):19–33.

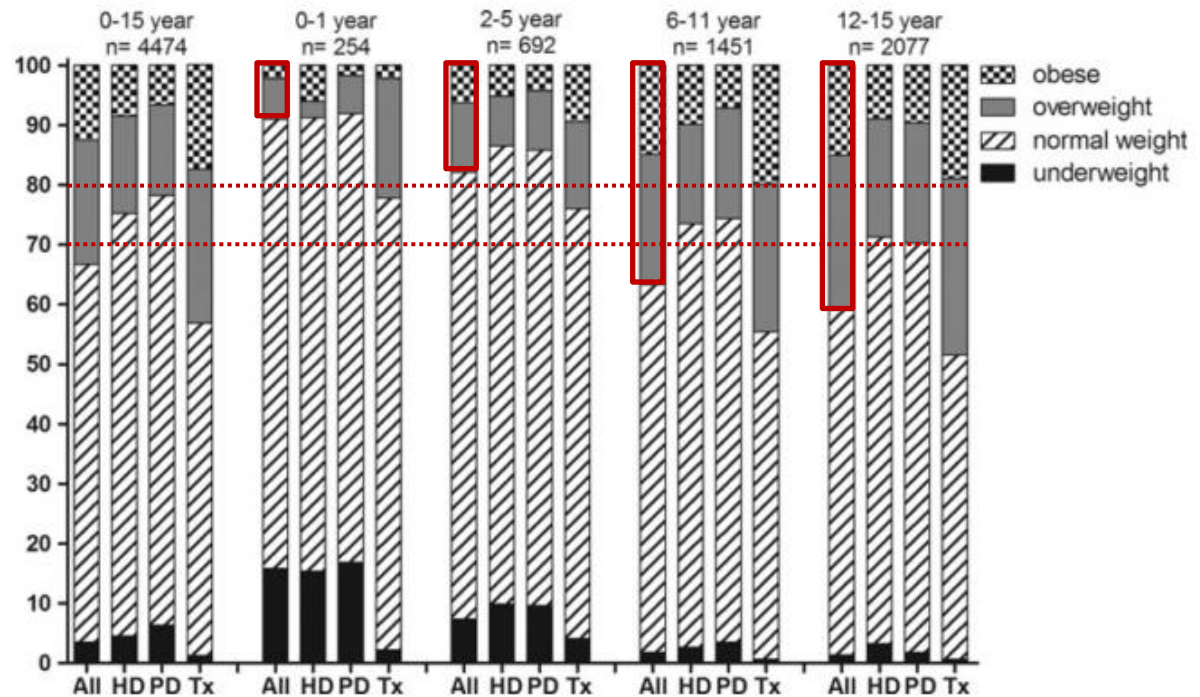


Kramer HJ et al, J Am Soc Nephrol 2006;17:1453–9.



Yoshida T et al, Intern Med 2008;47:1859–64.

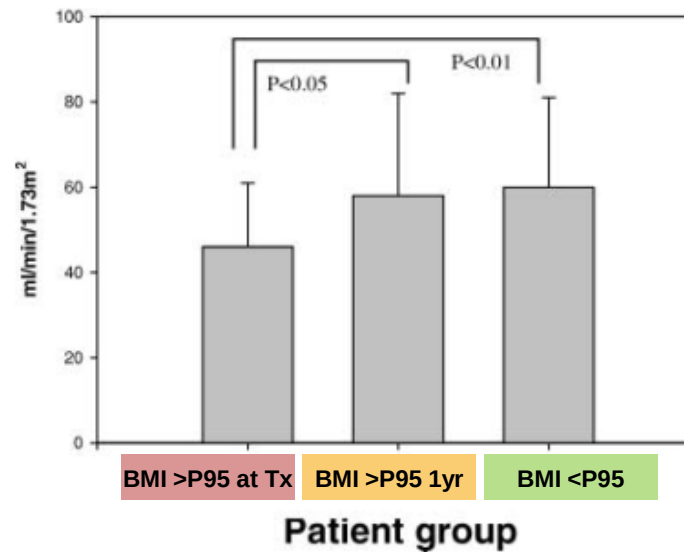
European pediatric population on renal replacement therapy (2013)
> 30% overweight/obese



Bonthuis M et al, Nephrol Dial Transpl 2013; 28 Suppl 4:iv195–204.

GFR at 1 year after renal transplantation (n=76 children)

Pre-transplant obesity → Lower GFR / Higher allograft dysfunction rate



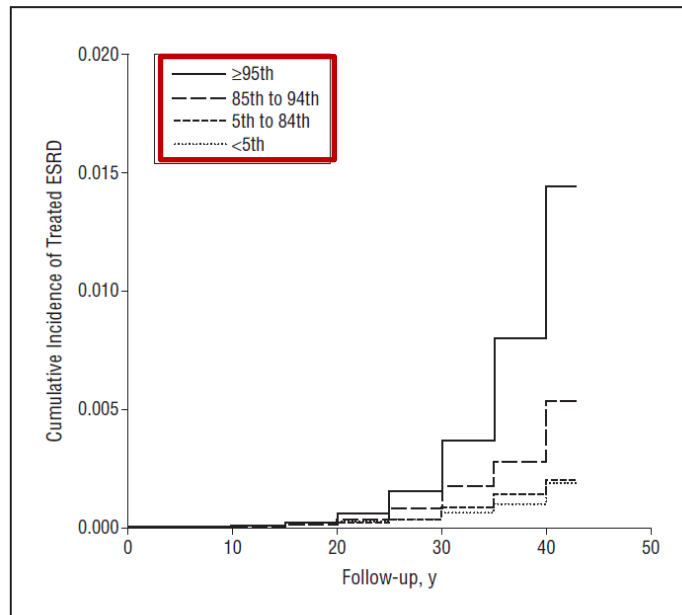
Mitsnefes MM et al. Pediatr Nephrol 2002;17:535–9.

Parece existir algum grau de **lesão renal associado à obesidade na infância**

Wahba IM et al, Clin J Am Soc Nephrol 2007; 2(3):550–62.

Obesidade infantil contribui para um aumento da **incidência de doença renal crônica**

Savino A et al, Horm Res Paediatr 2010; 73(5):303–11.

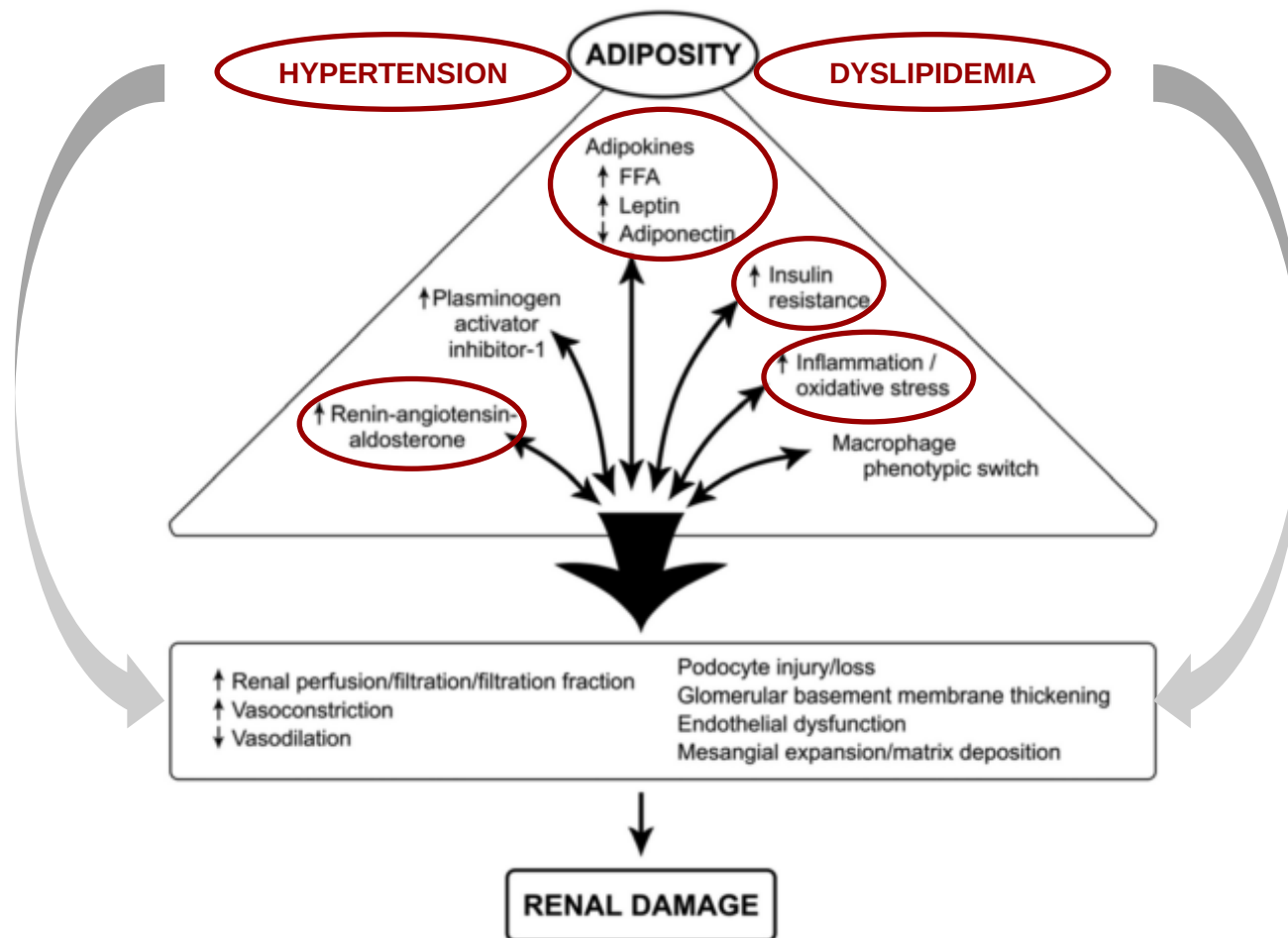


**Adolescentes com excesso peso/obesidade
Maior risco de DRC de qualquer causa**

Vivante A et al, Arch Intern Med 2012; 172(21):1644–50.

Silverwood RJ et al, Am J Kidney Dis 2013; 62(2):276–84.

Mecanismos de lesão renal induzida pela obesidade?



Mecanismos de lesão renal induzida pela obesidade?

Hiperfiltração

Adaptação fisiológica ao aumento de massa corporal e volume de sangue

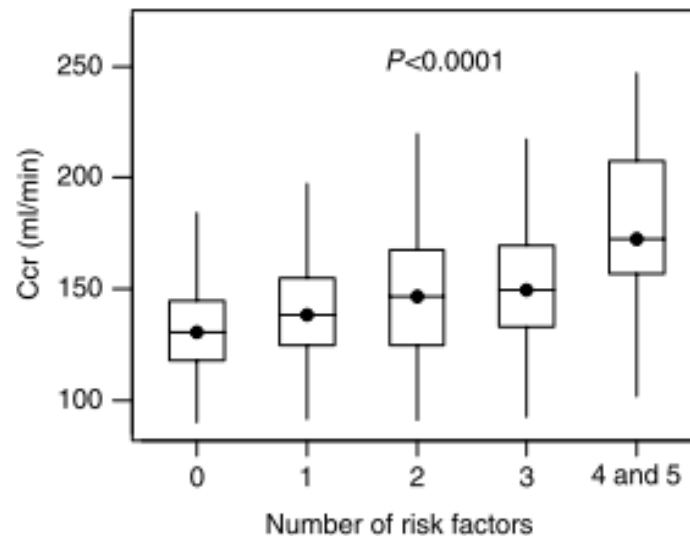


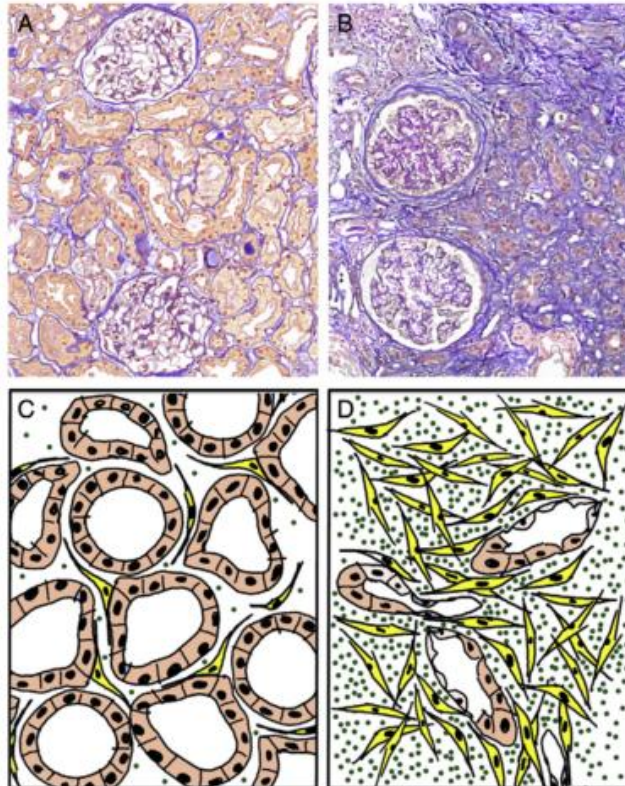
Figure 1 | Absolute creatinine clearance according to the number of metabolic risk factors.

Mecanismos de lesão renal induzida pela obesidade?

Hiperfiltração

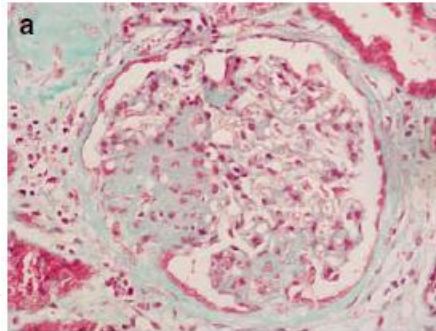


Remodelação tecidular

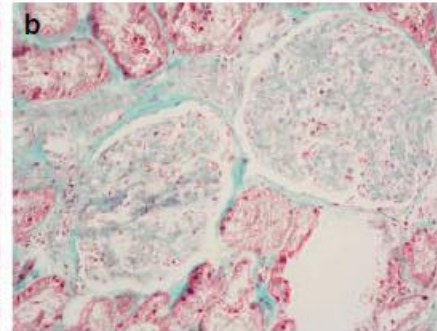


Glomerulopatia da obesidade

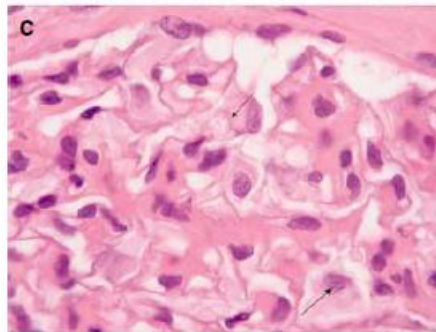
Lesões escleróticas periféricas



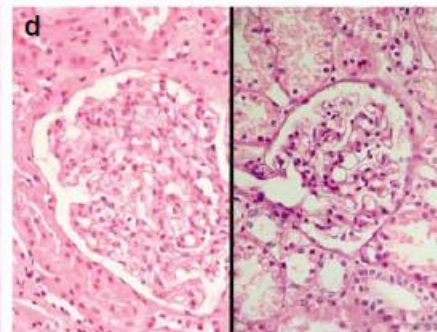
Aumento de matriz mesangial



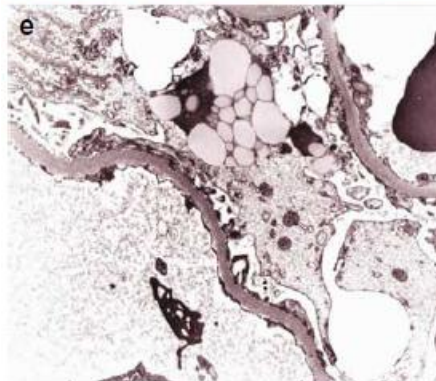
*Hipertrofia podocitária
com inclusões
citoplasmáticas de gordura*



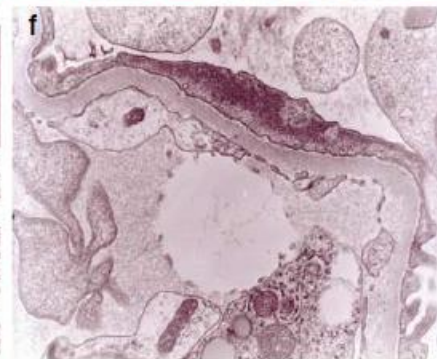
*Glomerulomegalia
(controlo da mesma idade)*



*M.E. – podócito com lípidos
intracitoplasmáticos e fusão
dos prolongamentos*



*Fusão de podócitos e
condensação de filamentos do
citoesqueleto*



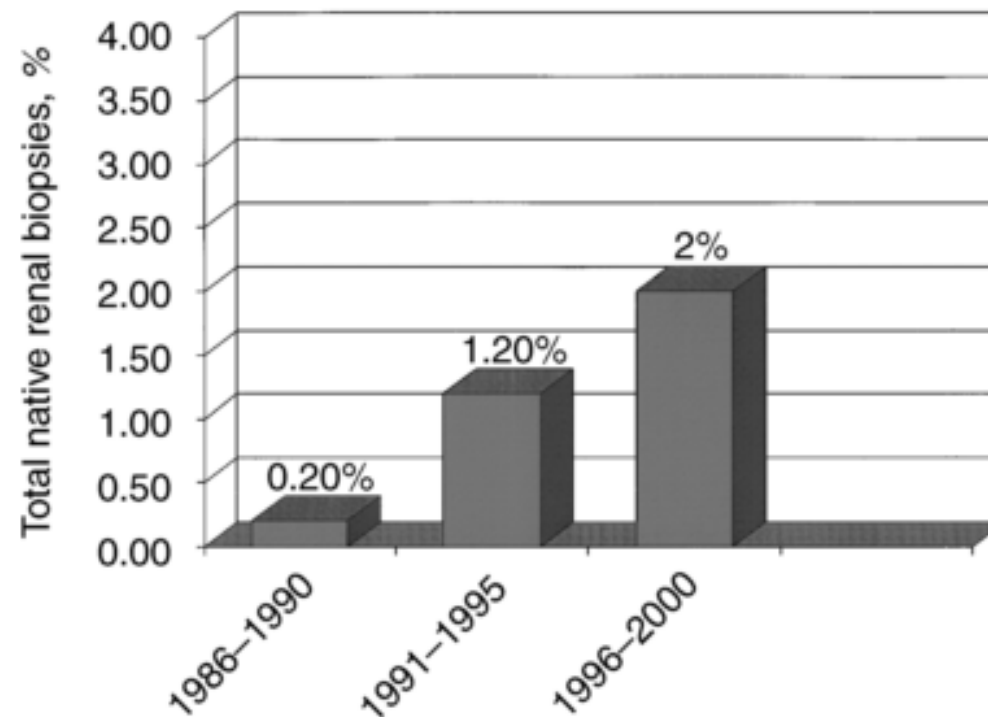
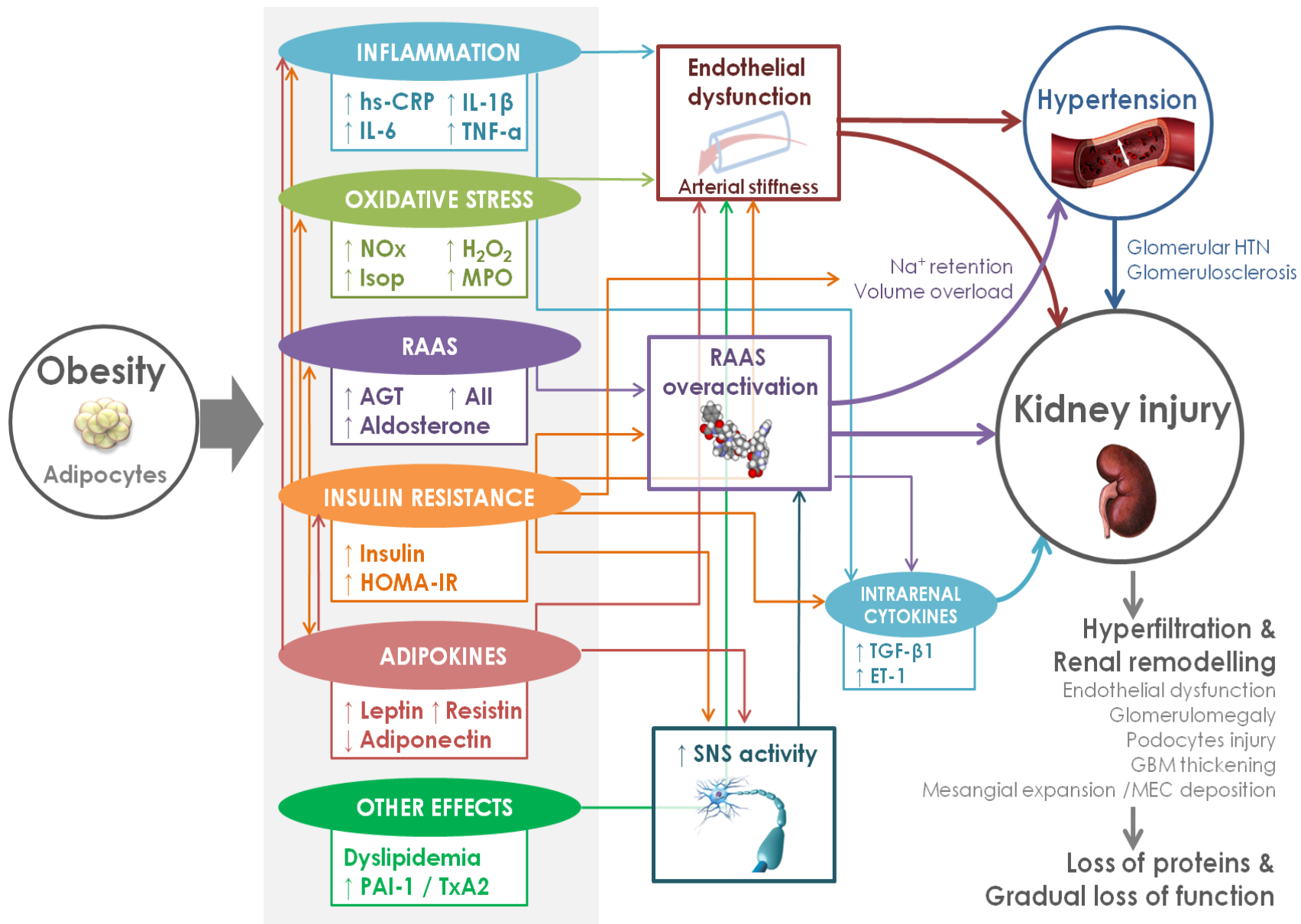


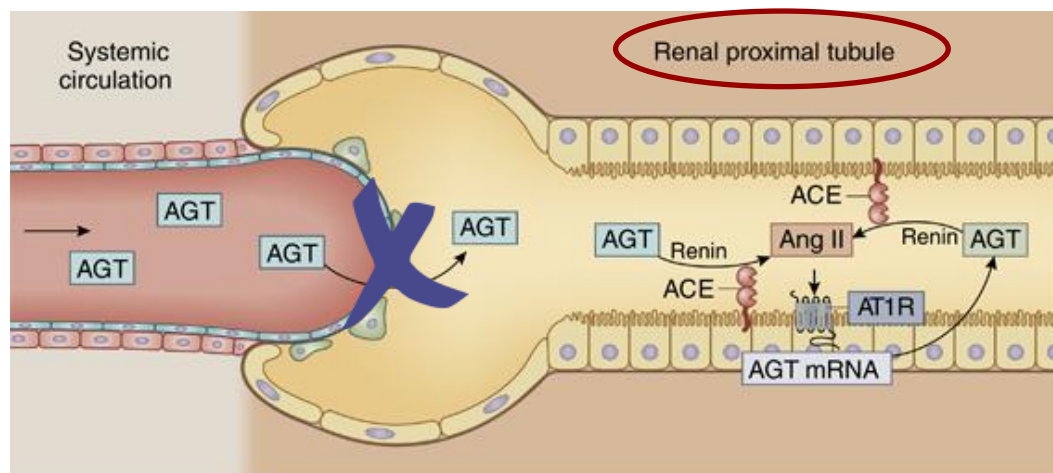
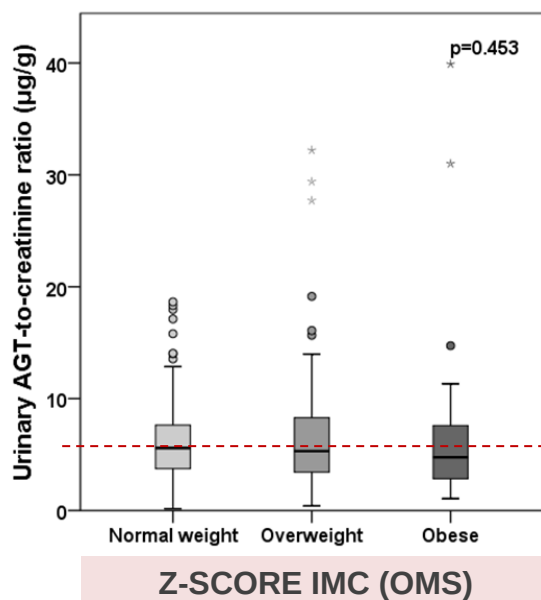
Fig. 1. The increased incidence of obesity-related glomerulopathy (ORG) is plotted as a percentage of total native renal biopsies received over a 15-year period.





SRAA

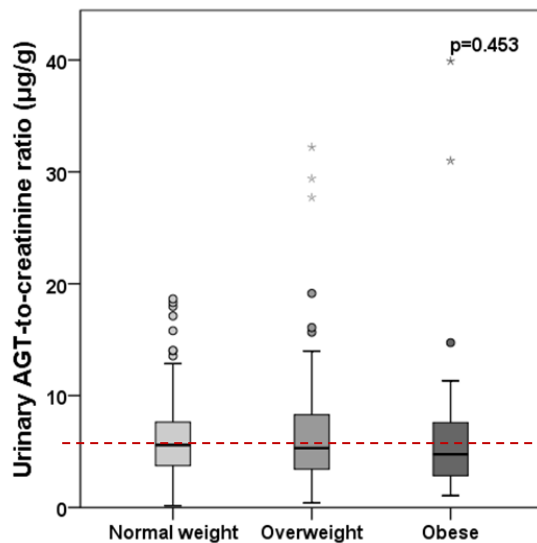
U-AGT



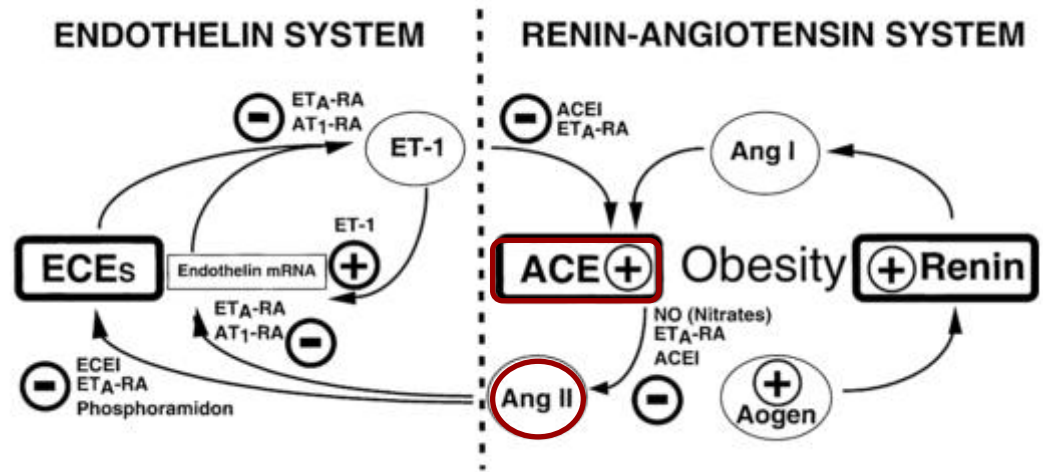
U-AGT = AGT produzido no TCP

SRAA

U-AGT



U-ET-1

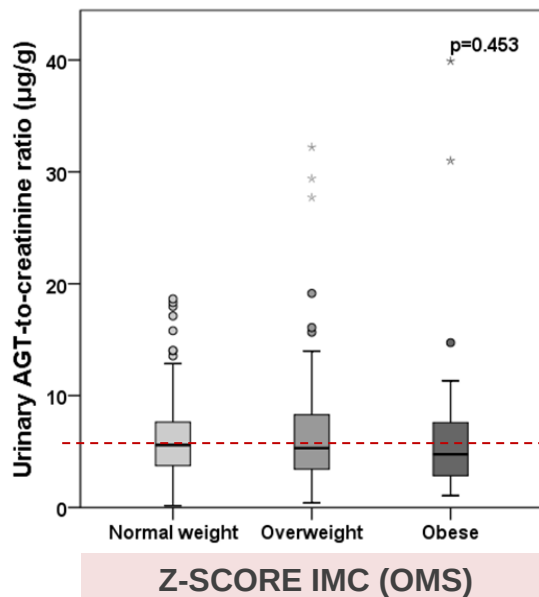


Reproduced from Barton M et al. *Int J Biochem Cell Biol* 2003;35:826–37.



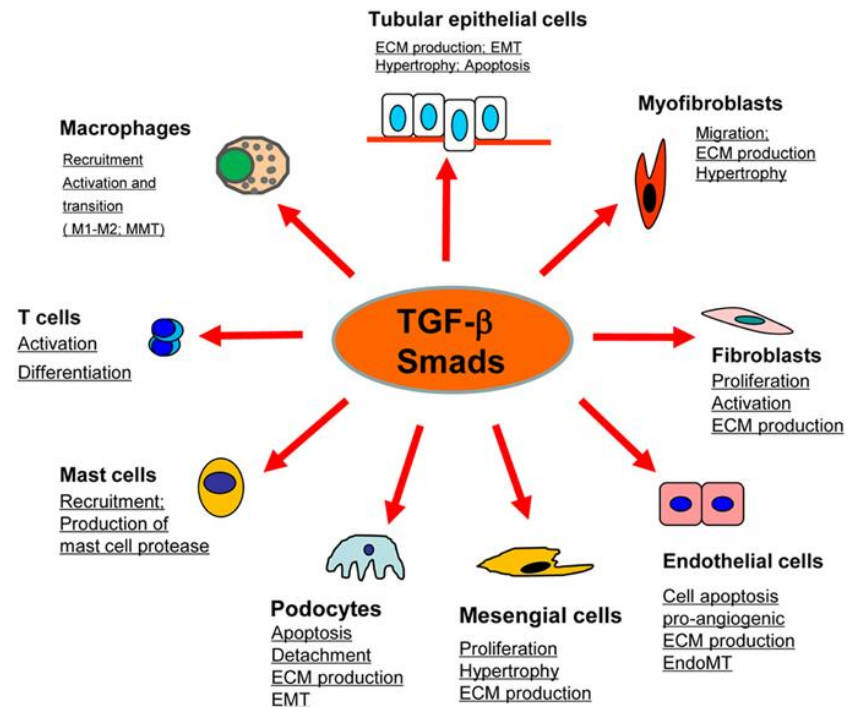
SRAA

U-AGT



U-ET-1

U-TGF- β 1



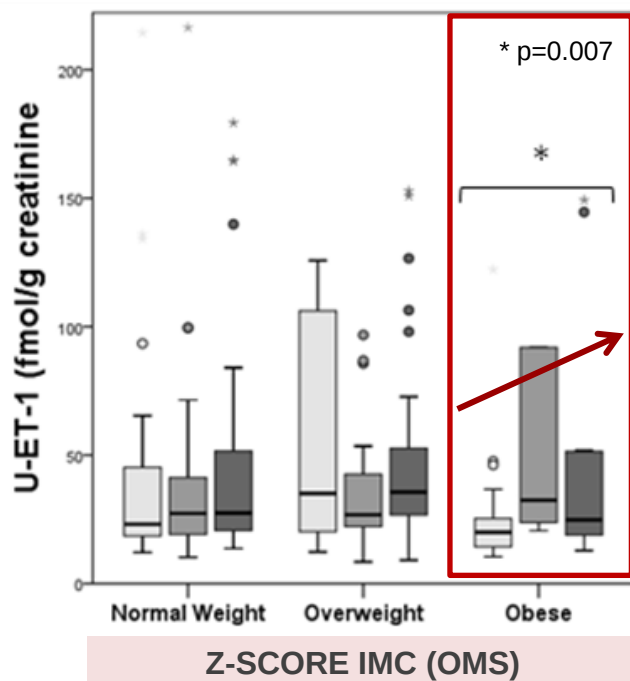


Projecto ObiKid

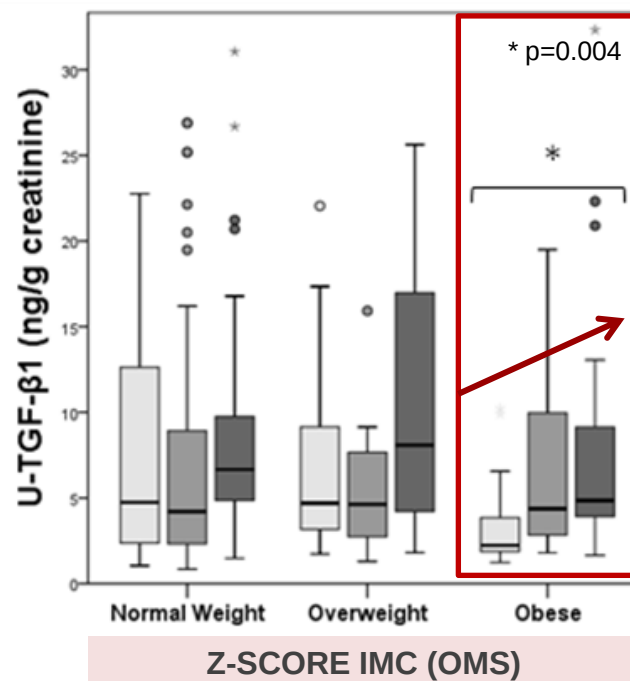
300 crianças 8-9 anos (150 excesso peso/obesidade)

SRAA

U-ET-1



U-TGF- β 1



U-AGT tertiles



Mecanismos de lesão renal induzida pela obesidade?

Remodelação tecidular



Proteinuria

Declínio função renal

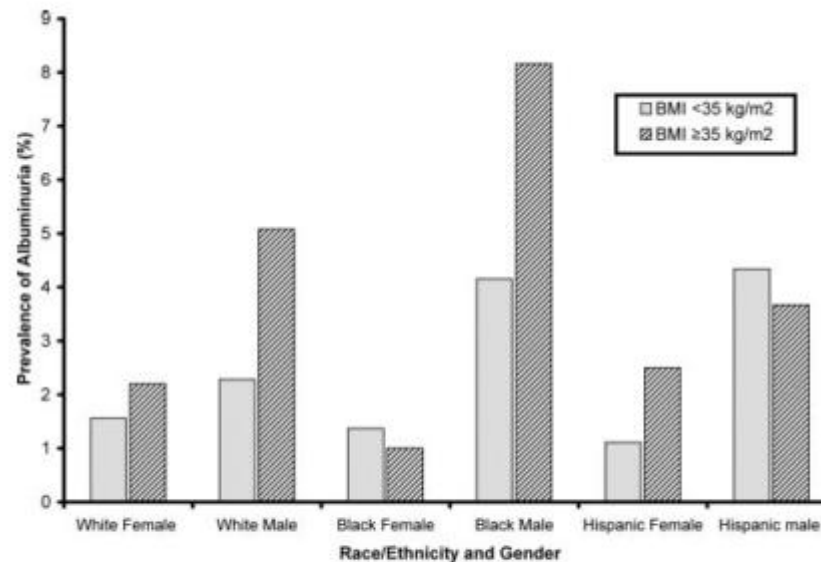
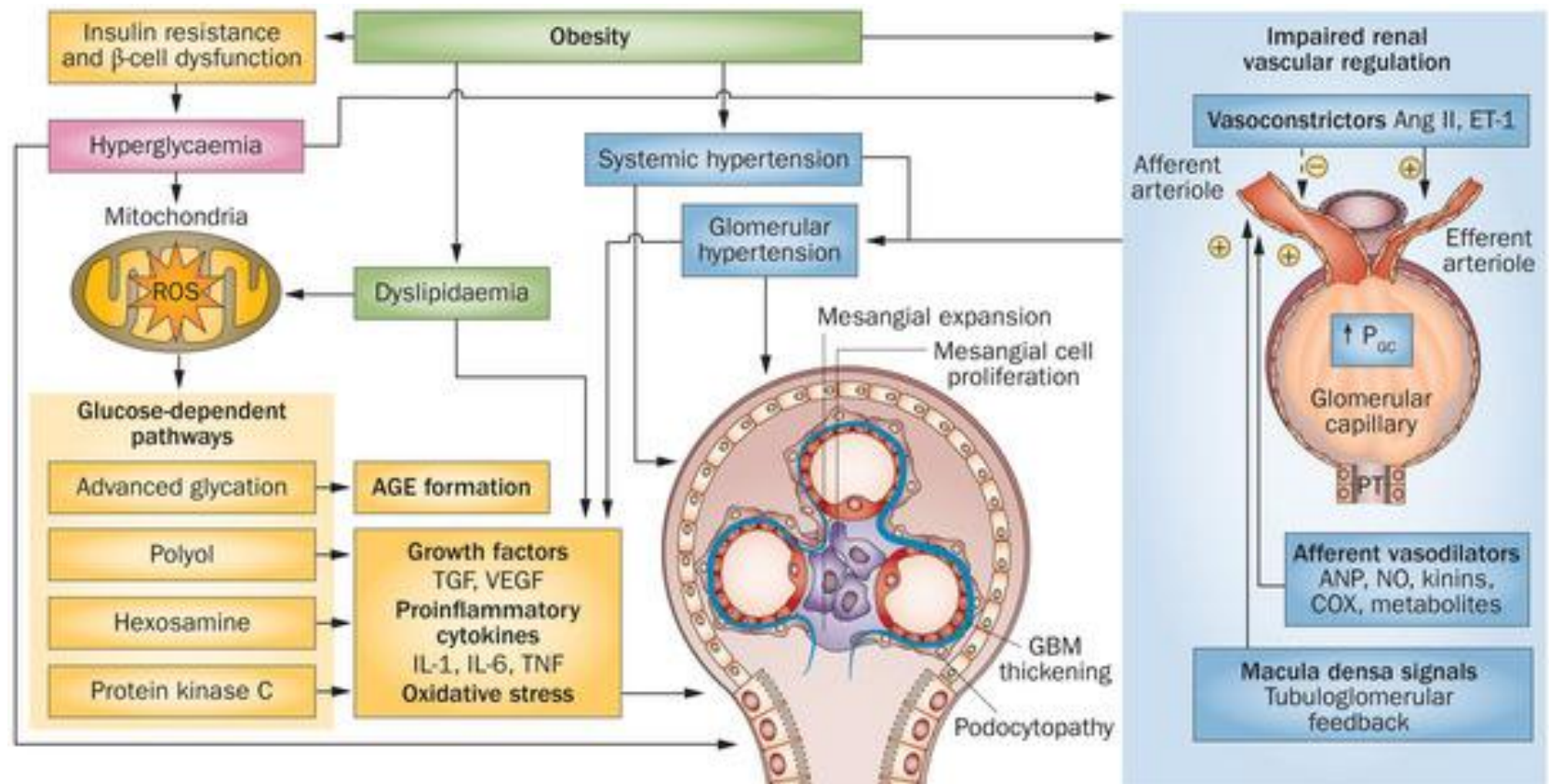


Figure 2. Prevalence of albuminuria (unadjusted) by class II obesity (body mass index [BMI] ≥ 35 kg/m²) versus all others (BMI <35 kg/m²) by race/ethnicity and sex groups.

Mecanismos de lesão renal induzida pela obesidade?



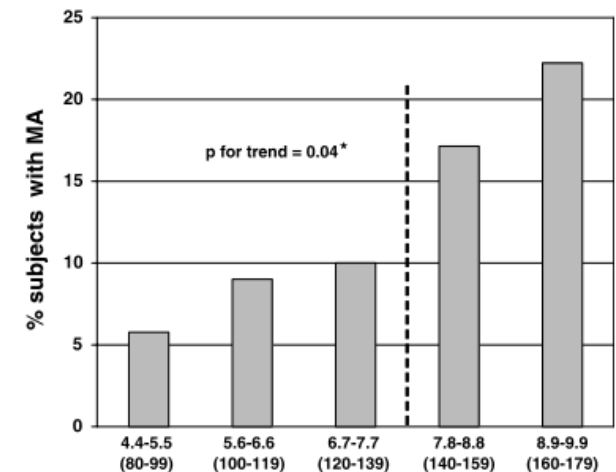
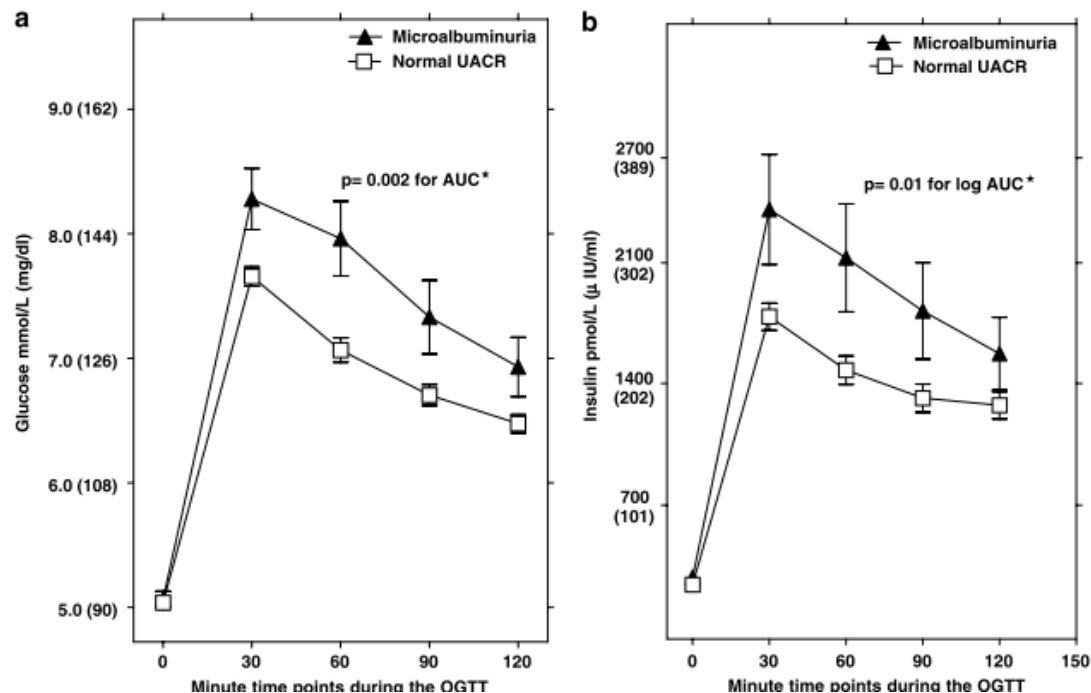
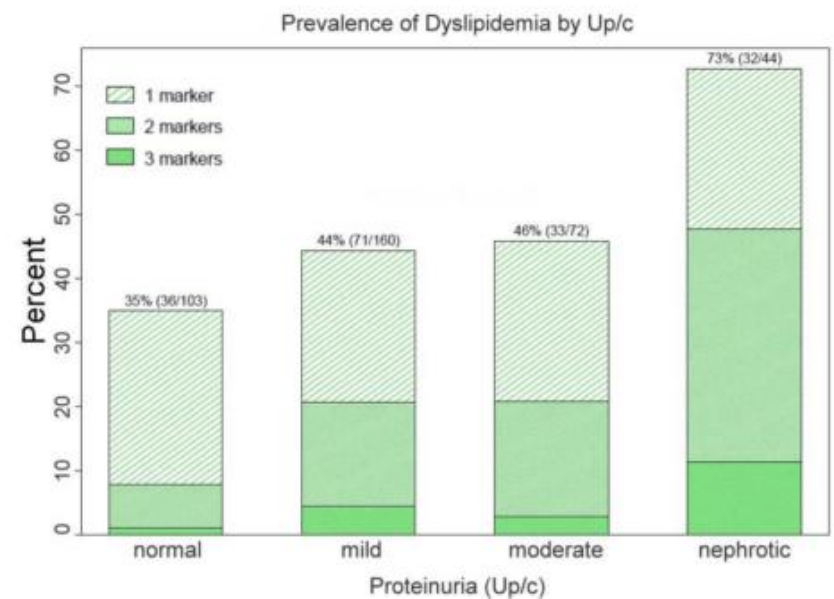
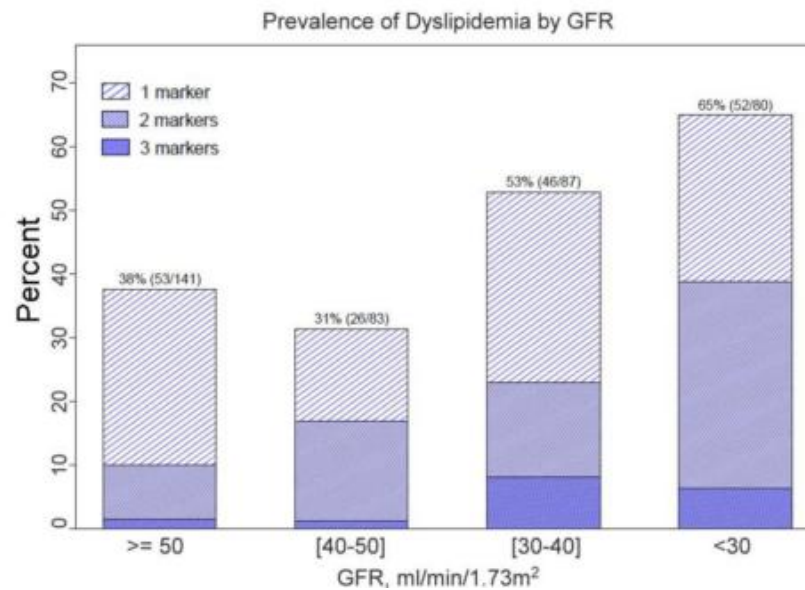
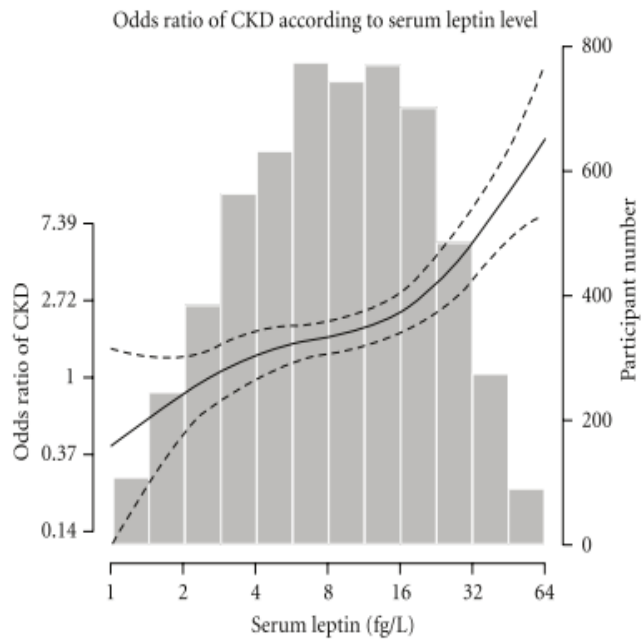
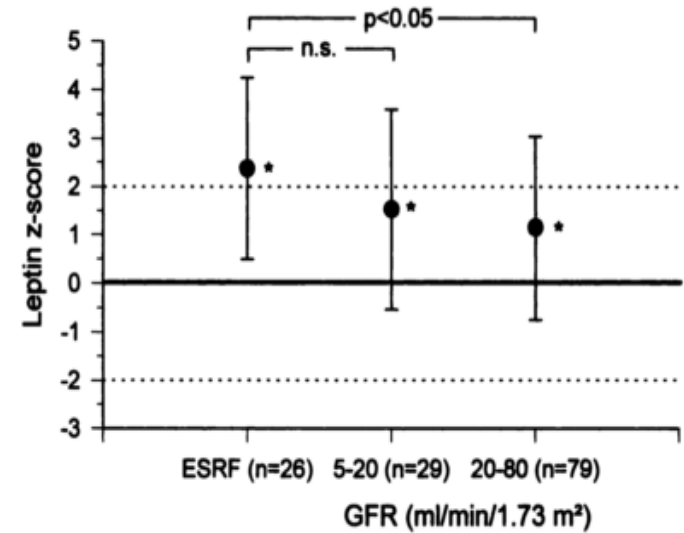


Figure 2 Relationship between % of subjects with a UACR in the microalbuminuric range and the 120 min plasma glucose levels after a standard oral glucose load. The dashed vertical line between the third and the fourth glucose quintile denotes the clinical threshold for the diagnosis of impaired glucose tolerance. *Adjusted for age, sex, BMI z-score and race/ethnicity.



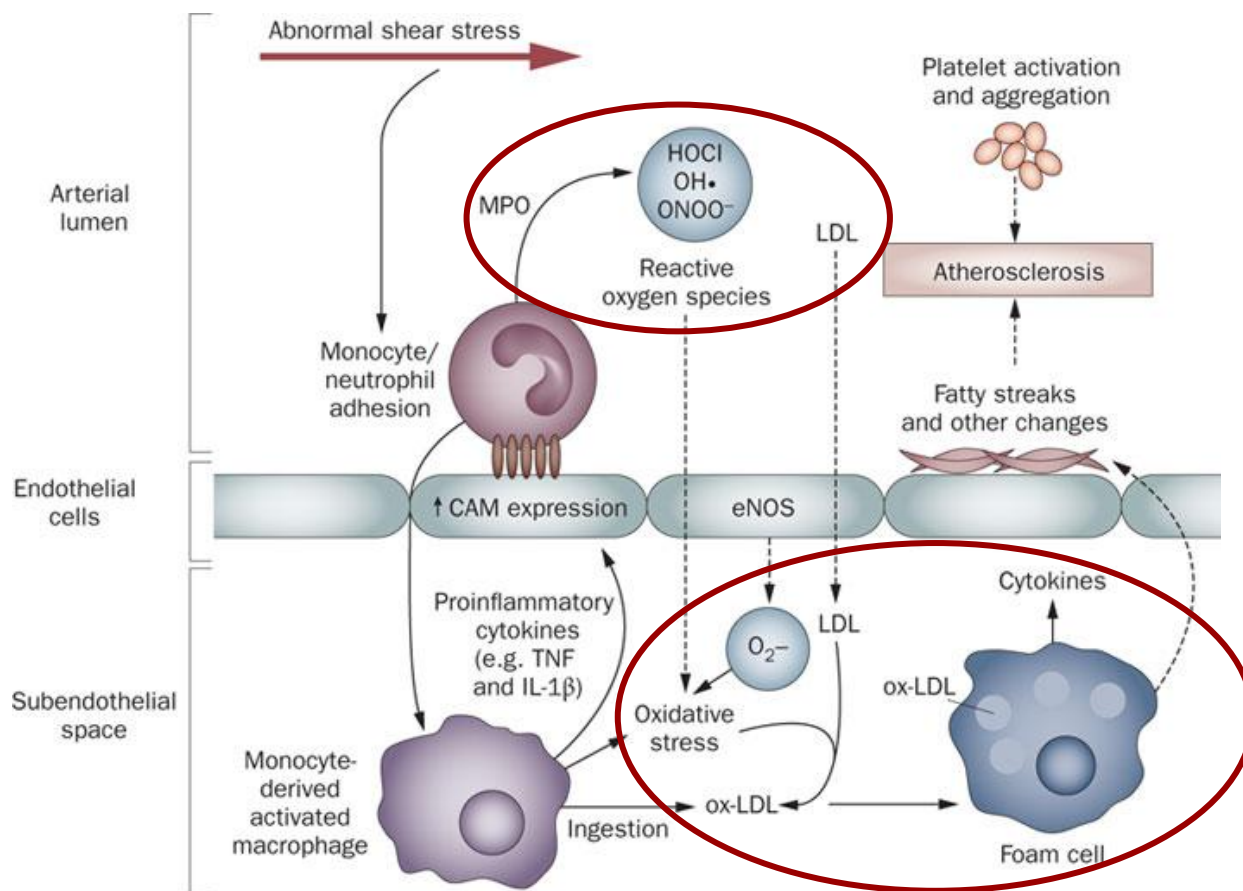


Shankar A et al, Int J Nephrol 2012;2012:269532.



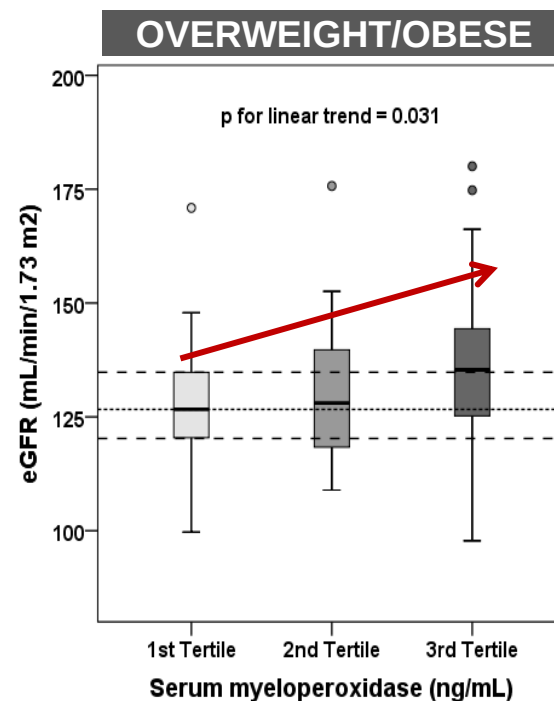
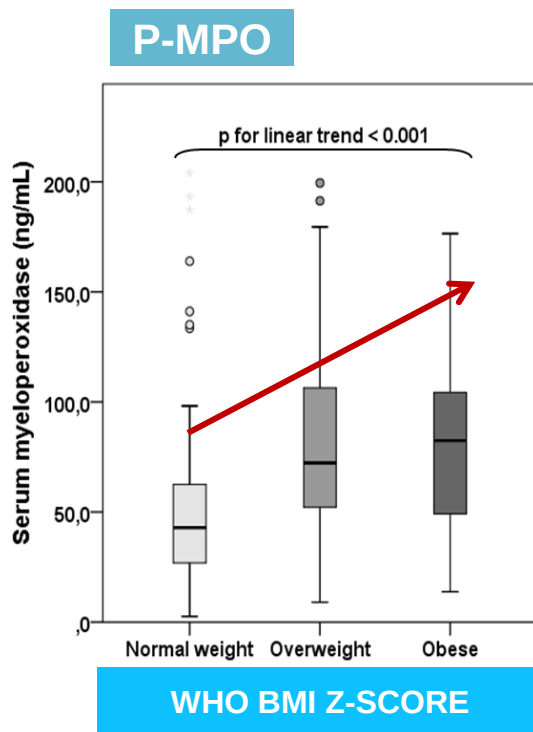
Daschner M et al, J Am Soc Nephrol 1998;9:1074–9.

Mieloperoxidase (MPO)



Myeloperoxidase as a Cardiovascular Biomarker in Prepubertal Children

Correia-Costa L, Sousa T, Morato M, Cosme D, Afonso J, Moura C, Mota C, Areias JC, Guerra A, Schaefer F, Caldas Afonso A, Barros H, Albino-Teixeira A, Azevedo A

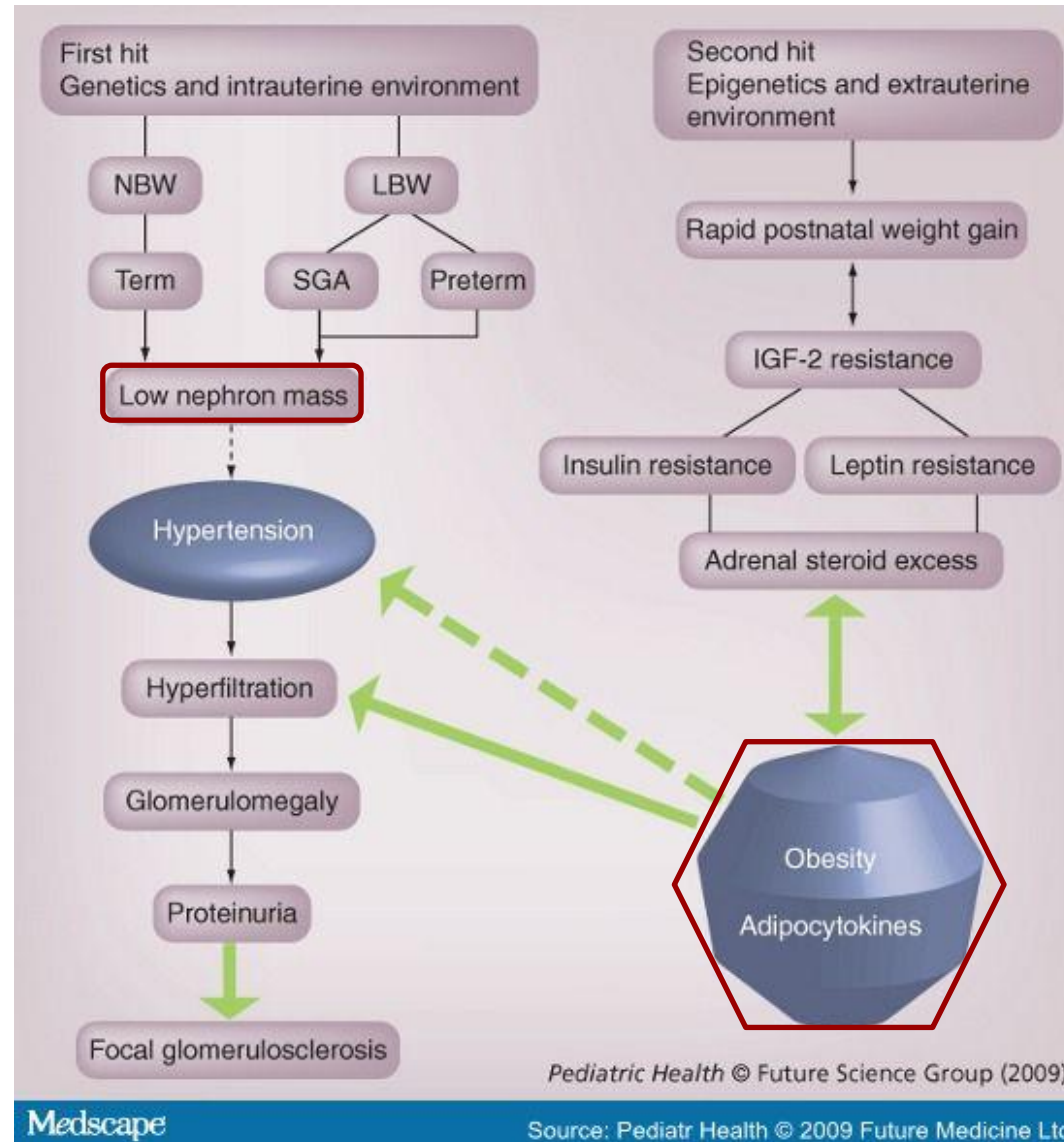


↑ eGFR across tertiles of MPO
 ↑MPO ↔ Hyperfiltration



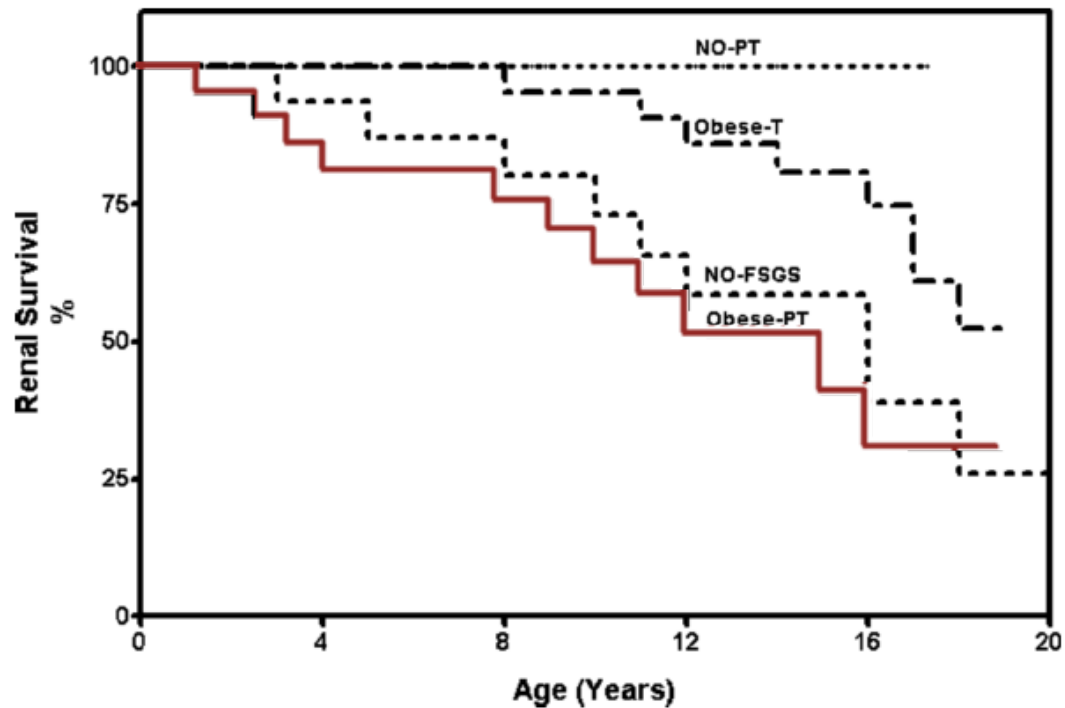


Determinantes perinatais de função renal





Determinantes perinatais de função renal



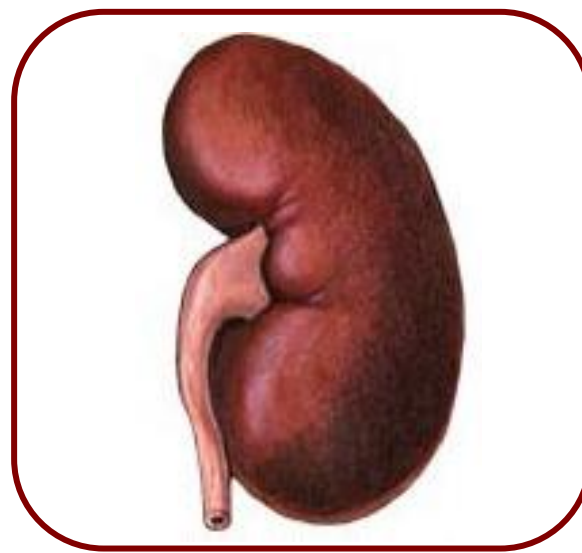
Reproduzido de Abitbol CL et al. *Pediatr Nephrol* 2009;24:1363–70.



***(Over) weight does matter
already in (early) childhood
even if overt consequences
will manifest only at later age***



1. **Combater obesidade** de forma a reduzir a carga de doença renal crónica
 - Prevenção e modificação de estilo de vida (alimentação / sal / exercício)
2. Avaliação frequente de **pressão arterial** (realizar MAPA 24 horas)
3. Avaliar a presença de **dislipidemia e IR**
4. Identificação precoce de **microalbuminuria**
5. Identificar factores de risco de **redução de massa de nefrónios**
6. Se possível, avaliar **marcadores de dano vascular (VOP)**
7. Iniciar **tratamentos que retardem a progressão de dano renal**
 - Redução de peso / Inibição do SRAA
 - Novos tratamentos? Alvos específicos? Adipocinas? Inflamação? Stress oxidativo?



ALL THOSE FAT YEARS

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Liane Correia-Costa

Hospital Pediátrico Integrado, Centro Hospitalar São João – Porto, Portugal



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15º CONGRESSO NACIONAL DE PEDIATRIA
Albufeira, 23 de Outubro de 2015