Obesity and the kidney

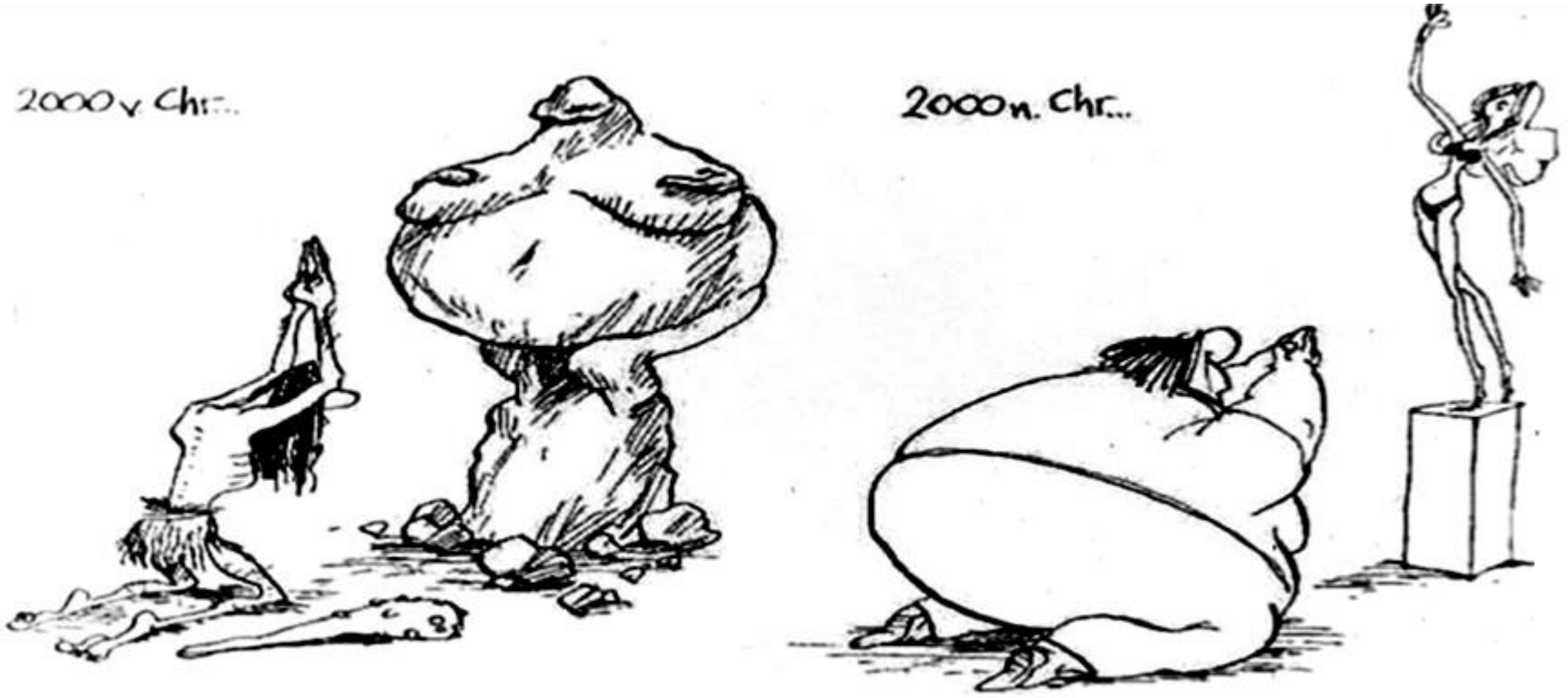
Eberhard Ritz
Heidelberg (Germany)

Obesity –
an ancient German tradition

Venus vom “Hohlen Fels“

female figurine of mammoth ivory; 35,000 years B.C. (Aurignacien); Schelklingen (Württemberg)

The relation of “body mass index“ between adoree and adorer has changed in the course of history



Obesity and the kidney

Venus of Willendorf (Austria) 4000 BC

- **Epidemiology of CKD and ESRD in obesity**
- **Renal morphology and function in obesity**
- **Role of visceral obesity**
- **Reversibility of renaL pathology in obesity**
- **Renal consequences of bariatric surgery**
- **“Obesity” – always detrimental ?**
  (“one body weight is optimal for all?”)

Body mass index (BMI) at age 20 years – important determinant of CKD risk at adult age

Risk of advanced CKD (S-creatinine > 3.4 mg/dl)

Swedish country wide "case control" study

BMI (kg/m^2)	odds ratio	
	Men	**Women**
< 25	**1.0**	**1.0**
> 25	**3.1** *(2.1-4.8)*	**3.0** *(1.4-6.1)*

Ejerblad, J.Am.Soc.Nephrol. (2006) 17:1695

Onset of reduced renal function → depends on BMI

- **Framingham study**,

  1223 men, 1362 women, 43 years
- **1978-1982 vs 1998-2001**

- ***odds ratio : eGFR < 90 ml/min in the course of 10 years***

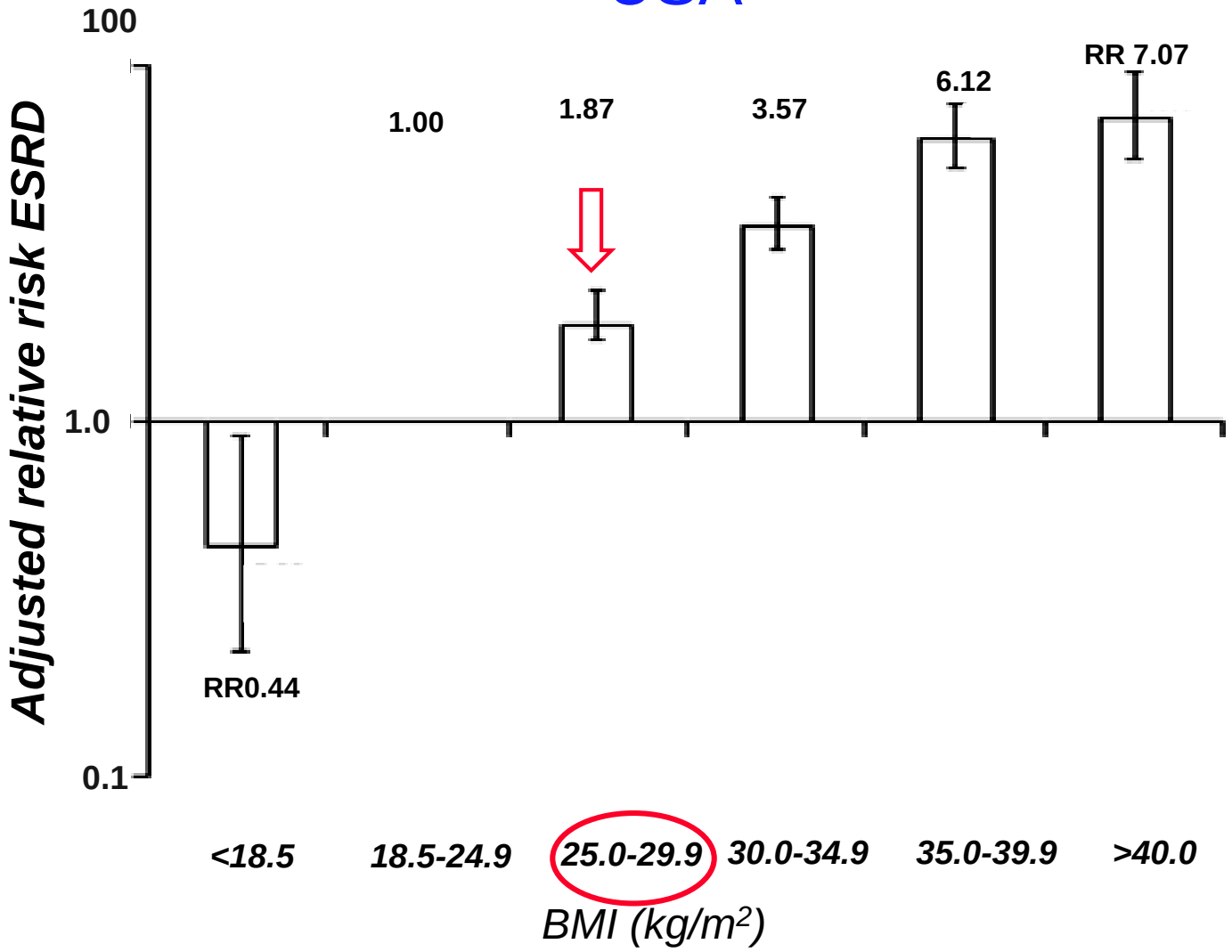
  - **age OR 2.3**
  - **diabetes OR 2.6**
  - **smoking OR 1.42**
  - **BMI OR 1.23 per 1 SD**

Fox, JAMA (2004) 291:844

BMI

independent predictor of "endstage renal disease"

USA



Hsu, Ann.Int.Med.(2006) 144:21

BMI

independent predictor of “endstage renal disease”

Europe

Obesity and chronic kidney disease

894 576 participants, 61% male, age 46 ± 11 years

hazard ratio per 5 kg/m² higher BMI

	15-25 kg/m²	***25-50 kg/m²***
Kidney Disease :	**1.14** ***(0.74-1.77)***	**1.59** ***(1.27-1.99)***
Diabetes :	**0.96** ***(0.59-1.55)***	**2.16** ***(1.89-2.46)***

Prospective Studies Collaboration, Lancet (2009) 373:1083

Risk of ESRD at obesity > 30kg/m²
higher in young as compared to elderly individuals

Risk underestimated in the elderlies? Cardiovascular death competing risk!

Hazard ratio

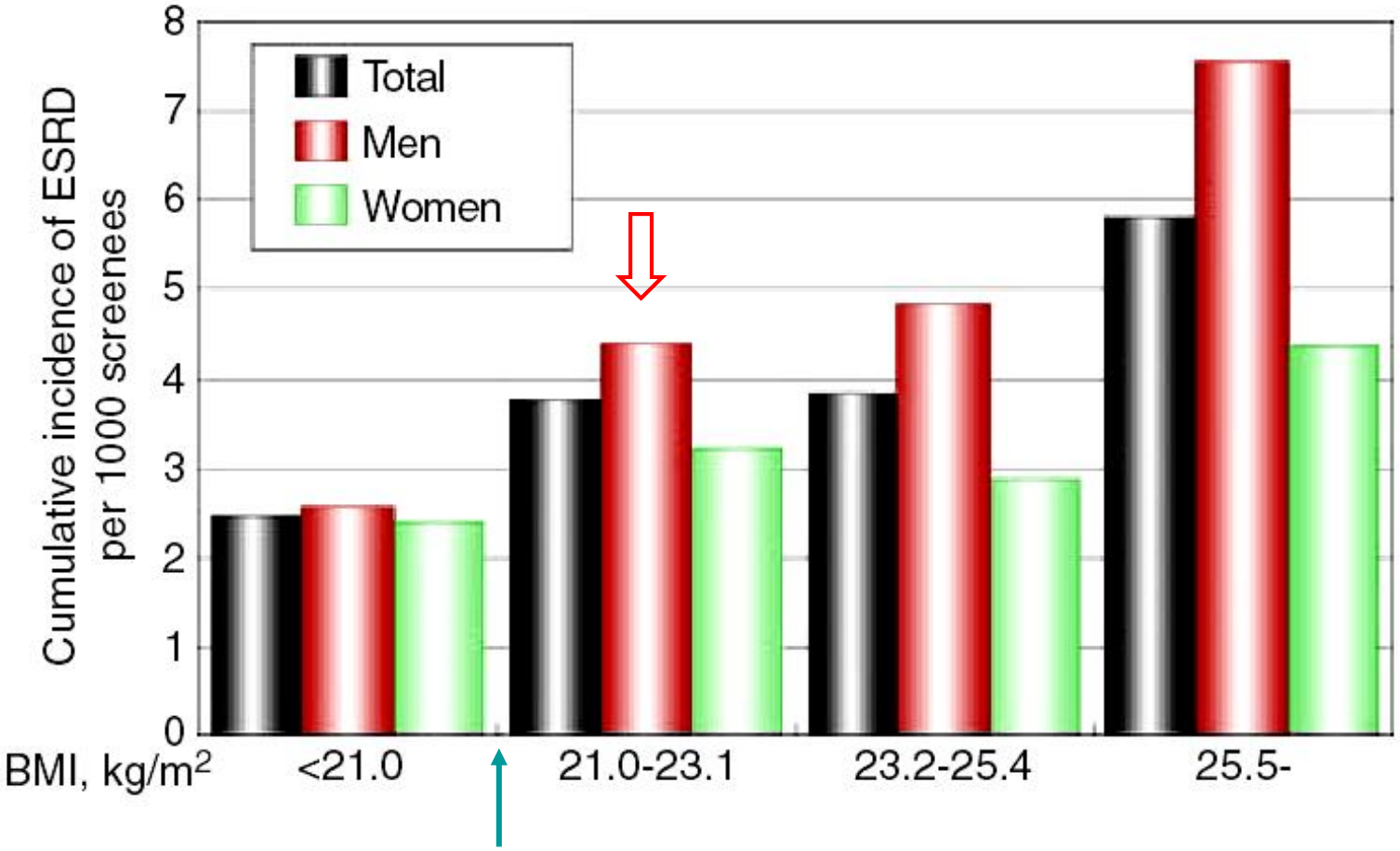
age	BMI (*kg/m²*) <18.5	18.5-24.9	25.0-29.9	30.0-34.9	35.0-39.9	>40.0
< 40 years	**0.2**	**1.0**	**1.8**	**4.4**	**7.3**	**11.6**
> 40 years	**0.8**	**1.0**	**1.9**	**3.1**	**5.5**	**4.8**

Hsu, Ann.Int.Med.(2006) 144:21

BMI

independent predictor of “endstage renal disease” (♂ > ♀)

Japan



Iseki, Kidney Intern (2004) 65: 1870

Obesity and Oxidative Stress Predict AKI after Cardiac Surgery

Frederic T. Billings IV,* Mias Pretorius,† Jonathan S. Schildcrout,‡ Nathaniel D. Mercaldo,‡ John G. Byrne,§ T. Alp Ikizler,‖ and Nancy J. Brown¶

JASN (2012) 23:1221

not only <u>chronic</u> kidney disease,

but also <u>acute</u> kidney disease :

"the relative risk of AKI increases significantly by 26.5% per 5 kg/m^2 (*p=0.02)*
compared to individuals with normal body weight
(BMI 18-24.9 kg/m^2) "

BMI : weaknesses

- **based on "fat mass" as well as "lean mass"** *(Sumo wrestlers)*
- **does not consider distribution of fat tissue** *(central vs peripheral)*

abdominal adiposity is associated with CKD –
independent of whether generalised adiposity is present or not
i.e. even isolated abdominal adiposity causes pathology

Kurella, J.Am.Soc.Nephrol.(2005) 16:2134
Lee, Am.J.Hypertens.(2007) 20:1189

does not reflect ectopic fat deposits in heart, vessels and kidney (sinus!)
in diabetic and nondiabetic individuals with CV disease

Montani, Int.J.Obes.Relat.Metab.Disord. (2004) 28(suppl 4)S58

Not all fat tissue is created equal : example "brown adipose tissue"

- **inversely correlated with BMI**

  Saito, Diabetes (2009) 58:1526
  Cypess, New Engl.J.Med.(2009) 360:1509

- **thermogenesis *(high energy – consumption)***

  Lowell, Nature (2000) 404:652

- **expression of UCP1** *(uncoupling protein)*
  e.g. thermogenesis induced by cold or diet

  van Marken, New Engl.J.Med.(2009) 360:1500

- **animal experiments: transplantation of "brown adipose tissue" ameliorates obesity and metabolic syndrome**

  Whittle, Trends Mol.Med.(2011) 17:405

Key abnormality : nonalcoholic fatty liver disease

Periphery:

- *(inflammation)*
- *(insulin resistance of fat cells)*
- *increased lipolysis* ⇨ *causes infiltration of liver by free fatty acids*

Liver:

Benign steatosis
- *diminished oxydation of fatty acids*
- *increased de novo lipogenesis (via hyperinsulinemia)*
- *disturbance of VLDL secretion*

Malignant steatosis
- *lipid oxidation (ROS)*
- *gut : # bacterial endotoxin*
  # short chain fatty acids
- *adipokine imbalance*

inflammation of visceral fat ⇨ *insulin resistance*

Stefan, Diabetes (2011) 60:2011
Hamad, Arab J.Gastroenterology (2012) 13:161

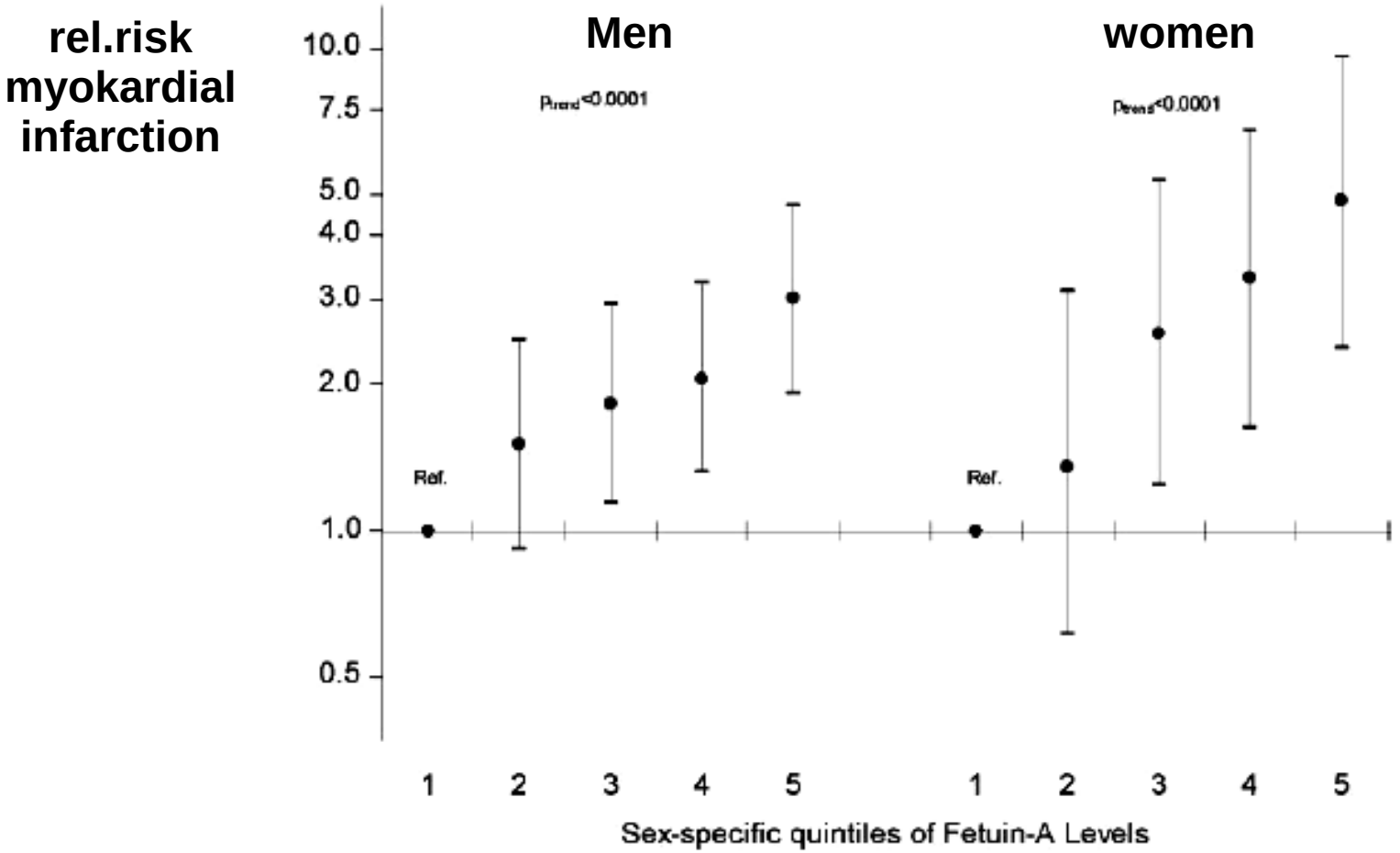
Plasma fetuin-A concentration and MI risk

(renal risk as well ?)

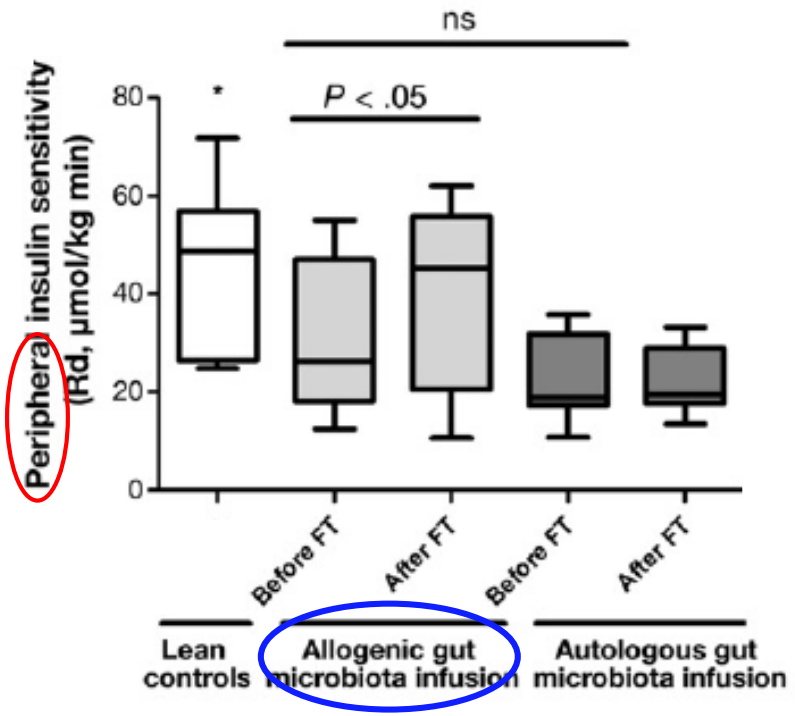
EPIC study

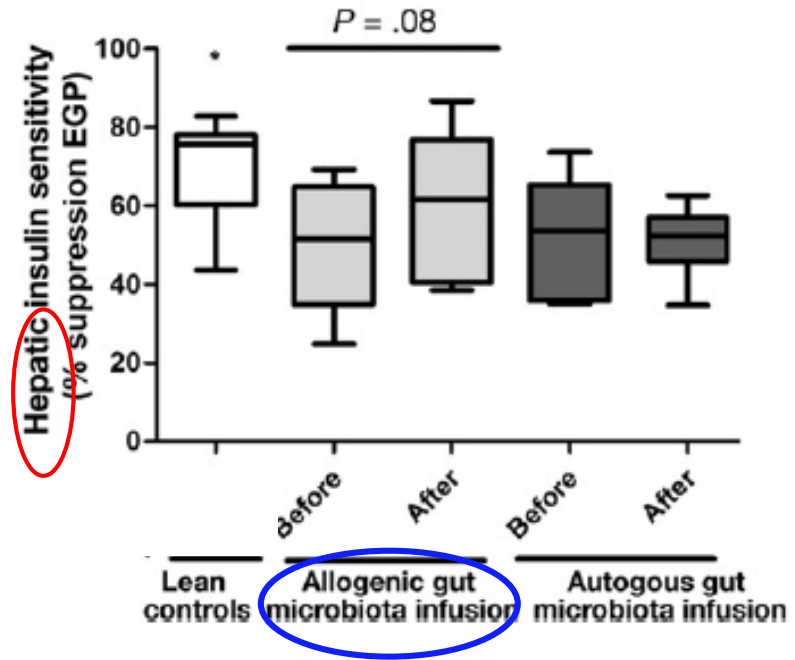
Fat liver is the culprit of : increased fetuin A synthesis

Fetuin A inhibits insulin receptor-tyrosinkinase → insulin resistance



Weikert, Circulation (2008) 118:2555



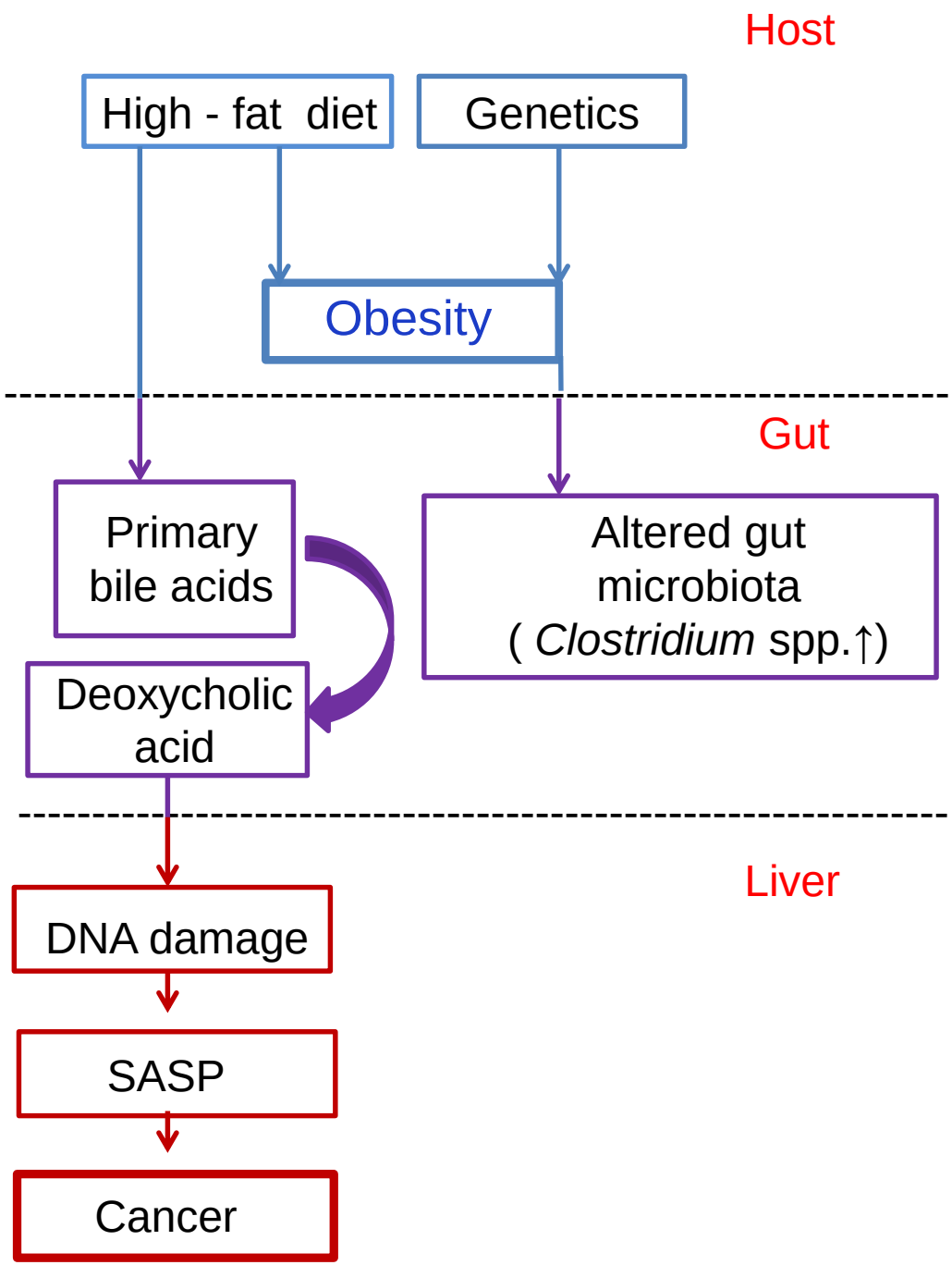


Unsavory ?

Transfer of
bacteria from colon of slim donors
into the duodenum of obese recipients
with metabolic syndrome

colonisation by clostridium difficile :
increase of
peripheral and hepatic insulin sensitivity
and
increased butyrate synthesis in the gut

Vrieze, Gastroenterology (2012) 143:913



Another example of sequelae of gut bacteria

Obesity-induced gut microbial metabolite promotes liver cancer through senescence secretome

Shin Yoshimoto,Tze Mun Loo,Koji Atarashi et al
Nature (2013)499:97

“Fatty kidney sinus“
prediction of renal risk
(Framingham Heart Study)

	Fatty kidney sinus *(n=879)*	No fatty kidney sinus *(n=2044)*	p
Systolic BP *(mmHg)*	**129 ± 17**	**120 ± 15**	*< 0.0001*
Diastolic BP *(mmHg)*	**75 ± 11**	**75 ± 9**	*< 0.0001*
Hypertension *(%)*	**57.8 %**	**26.6%**	*< 0.0001*
Diabetes *(%)*	**14.6 %**	**4.2%**	*< 0.0001*
$eGFR_{cystatin}$ *(ml/min/1.73m²)*	**81 ± 17**	**89 ± 16**	*< 0.0005*
CKD	**9.1%**	**2.8%**	*< 0.0005*

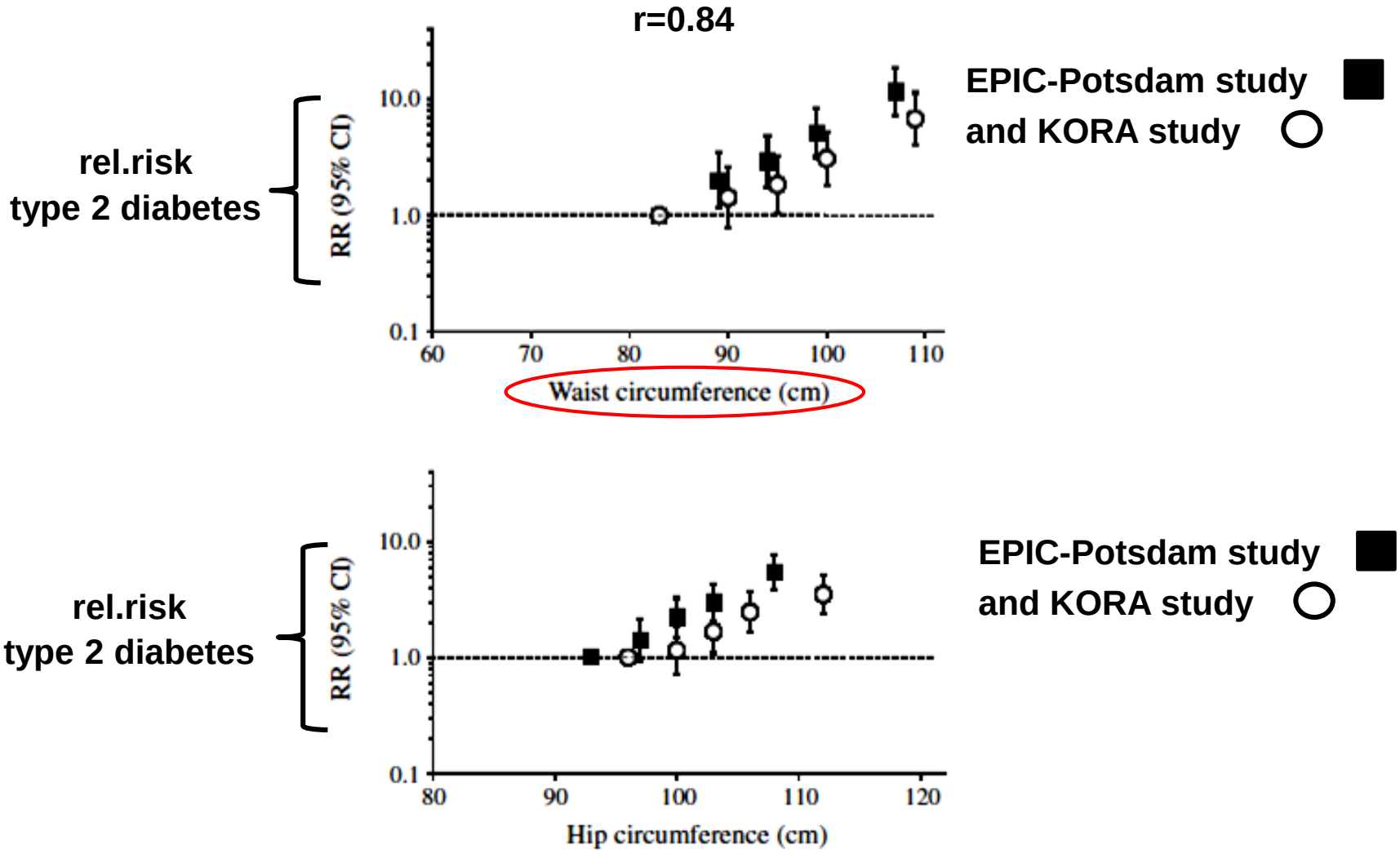
Foster, Hypertension (2011) 58:784

Assessment of body fat in men (and women)

⇨ *"waist circumference"*

***best* predictor of percent body fat (and onset of type 2 diabetes)**

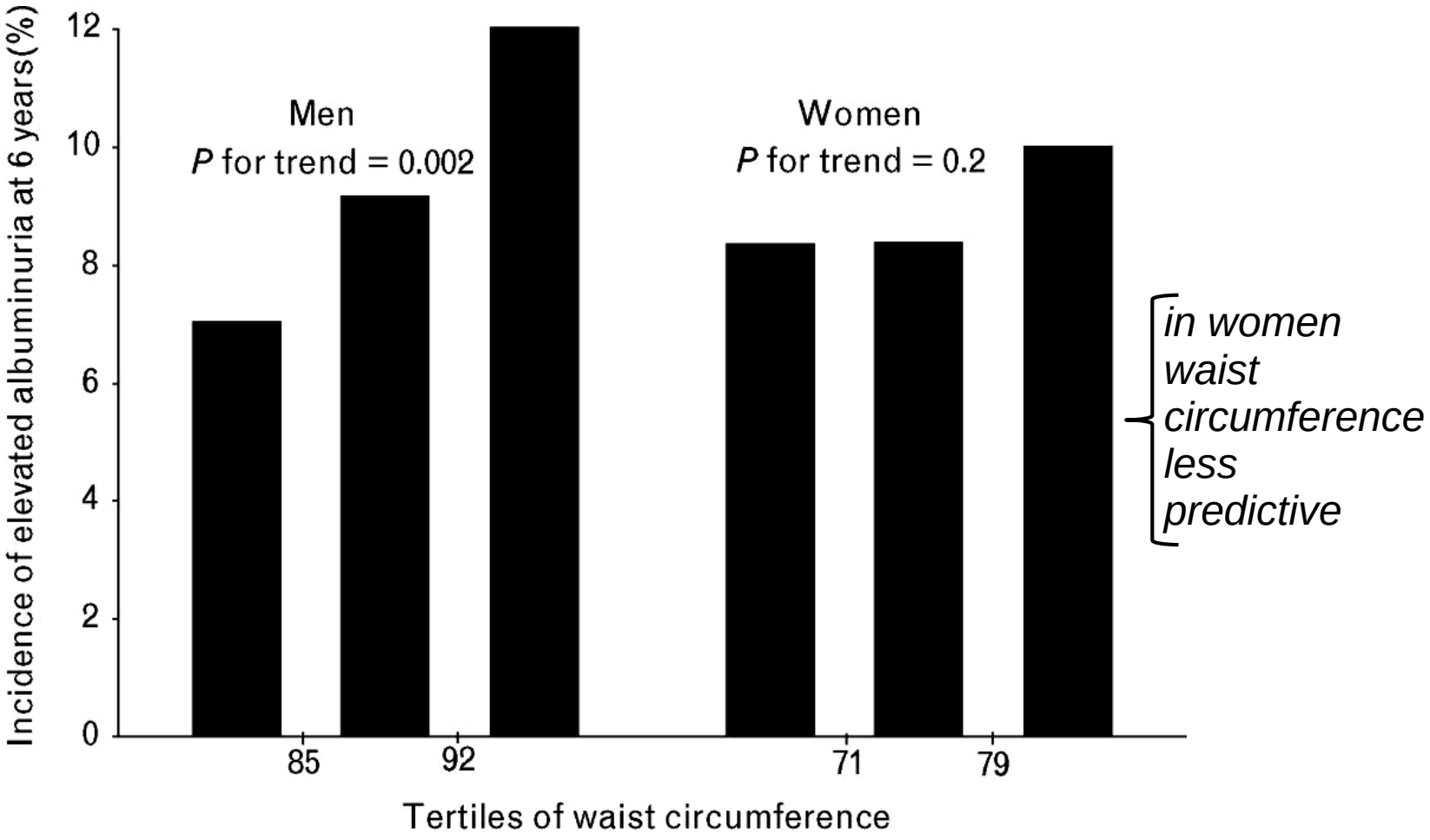
(validated by magnetic resonance tomography)



Schulze, Diabetologia (2012) 55:1660

6 year-incidence of microalbuminuria in non-diabetic individuals predicted by waist circumference

DESIR study



Bonnet, J.Hypertens.(2006)24:1157

Obesity and the kidney

Venus of Willendorf (Austria) 4000 BC

- **Epidemiology of CKD and ESRD in obesity**
- **Renal morphology and function in obesity**
- **Role of visceral obesity**
- **Reversibility of renaL pathology in obesity**
- **Renal consequences of bariatric surgery**
- **“Obesity” – always detrimental ?**
  (“one body weight is optimal for all?”)

Kidney in Obesity

Ritz, Semin.Nephrol.(2009) 29:504

 # renal problems caused by non-parenchymal kidney disease

(renal carcinoma, nephrolithiasis)

Adams, Am.J.Epidemiol. (2008)168: 268
Obligado, Am.J.Hypertens.(2008) 21:257

 # one specific form of primary kidney disease induced by obesity

(focal segmental glomerulosclerosis FSGS)

Weisinger, Ann.Int.Med.(1974)81:440
Kambham, Kidn.Internat,(2001)59:1498

 # worsening of prognosis of primary kidney diseases

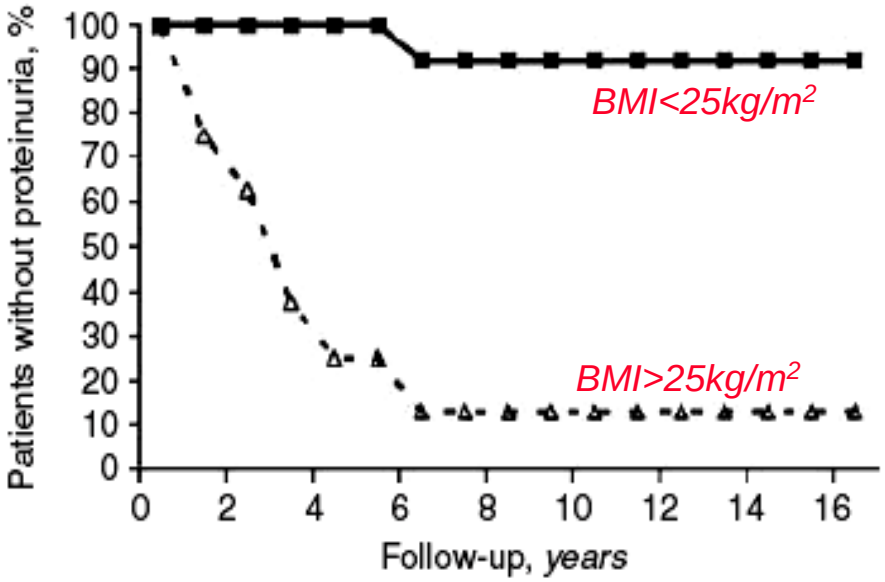
(uninephrectomy, IgA-GN, kidney-allograft, (pre)diabetic nephropathy …)

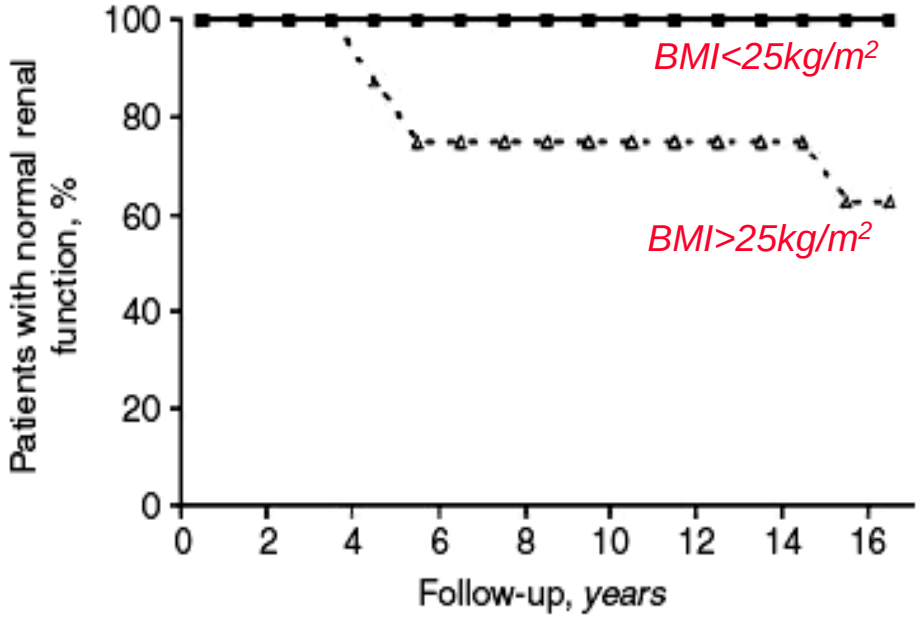
Gonzales, Kidn.Internat.(2005)68:263
Bonnet,Am.J.Kidn.Dis.(2001)37:720
Meier-Kriesche, Transplantation (2002)73:704
Altiparmak, Netherl.J.Med.(2002)60:260

Risk amplifier : uninephrectomy

Proteinuria and reduced renal function

in patients after uninephrectomy ⇨ depending on BMI





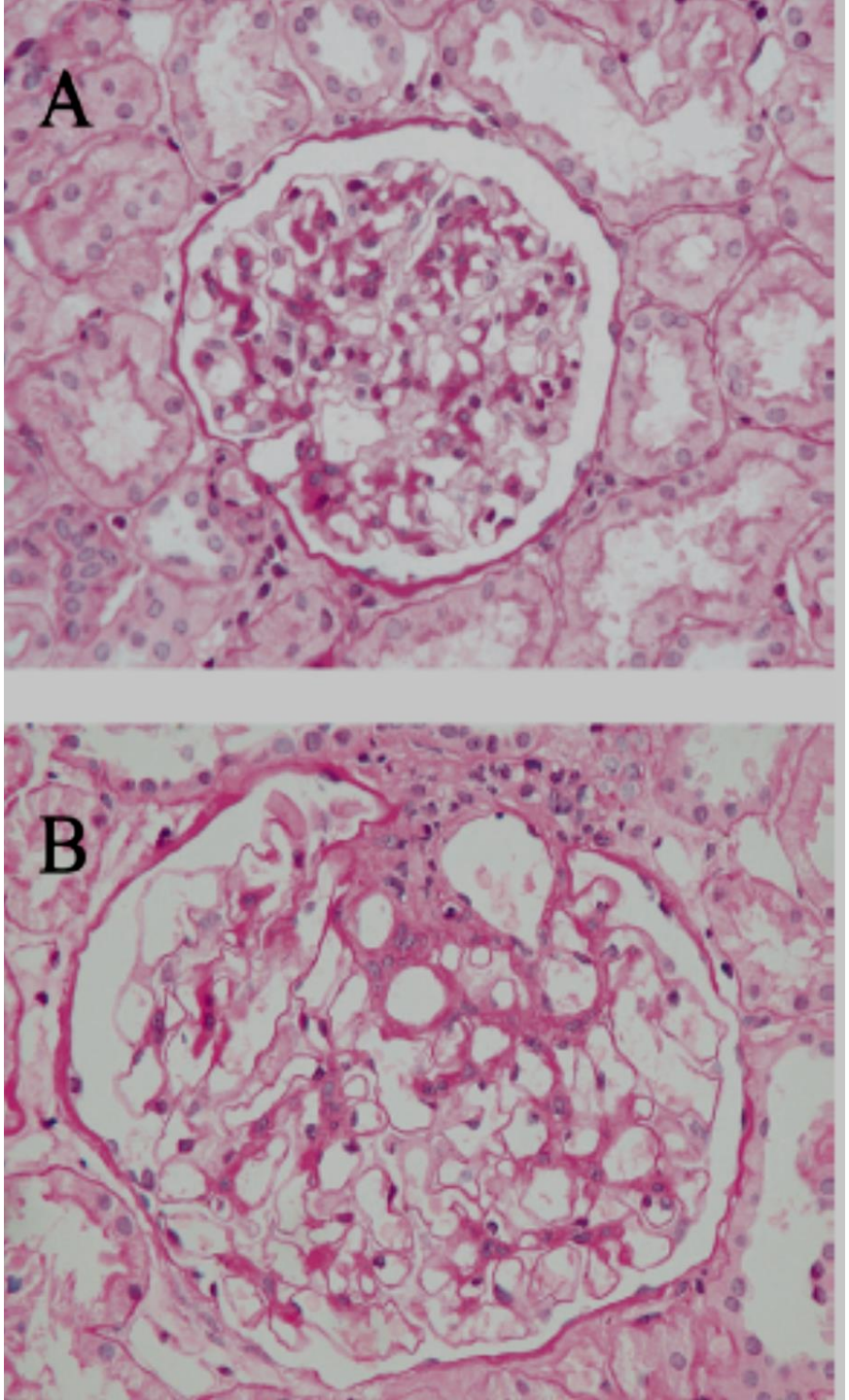
Gonzales, Kidn.Intern.(2005) 68:263

“Obesity related glomerulopathy”

⇩

Glomerulus :

hypertrophy
and
podocyte
pathology

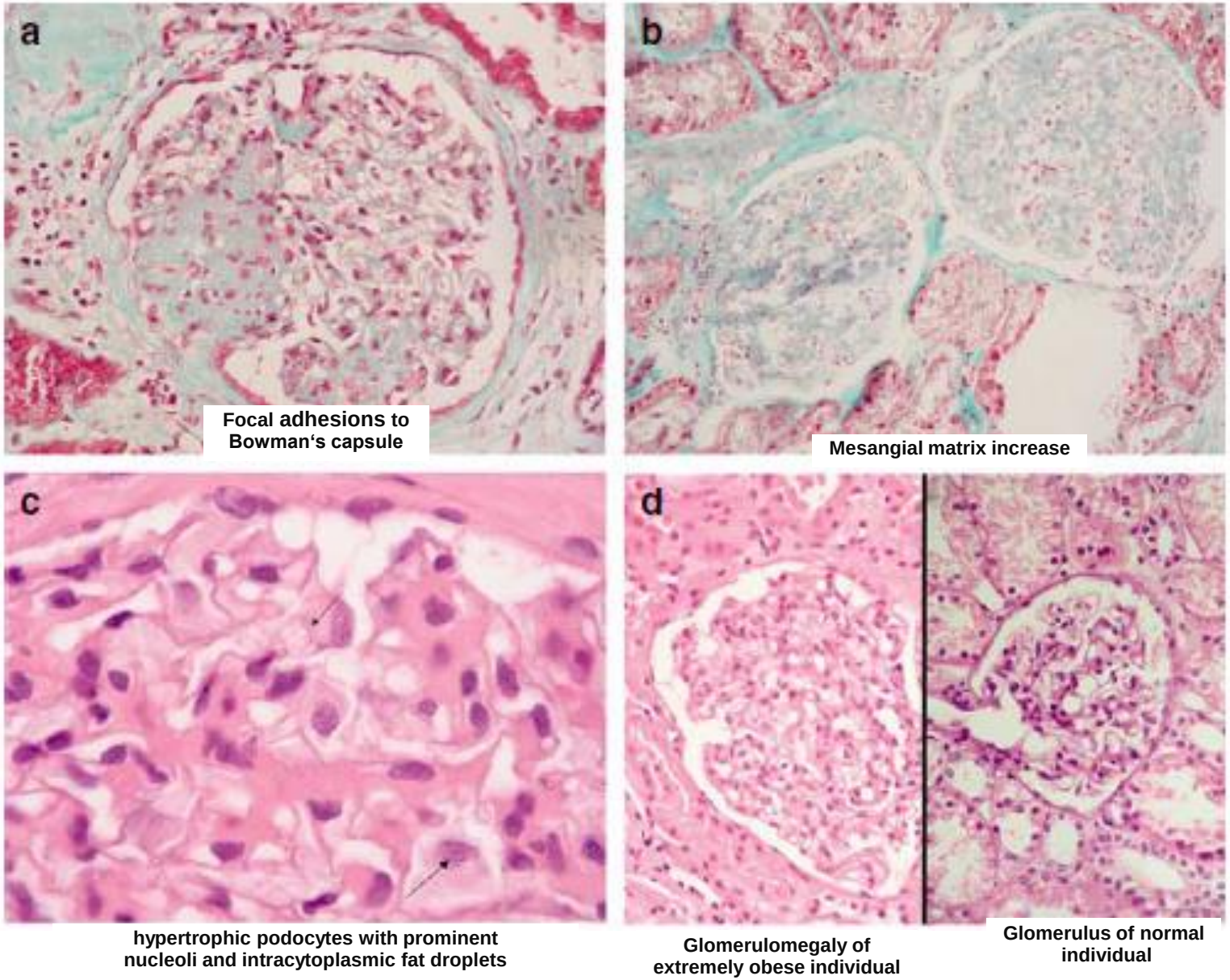


Control

Obesity

Chen,
AJKD (2006)48:772

Individuals with extreme obesity may have <u>major glomerular pathology</u> ⇨ <u>despite normal renal function</u>



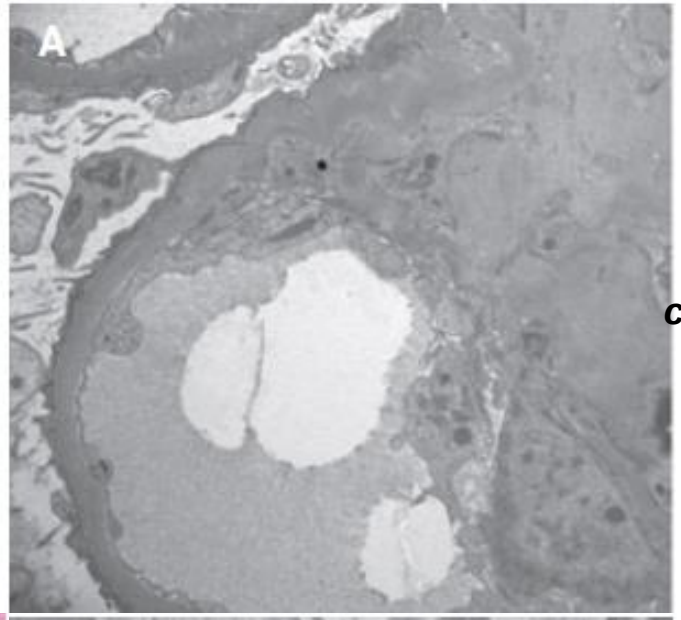
Serra, Kidn.Internat.(2008) 73: 947

Nodular Glomerulosclerosis (!)

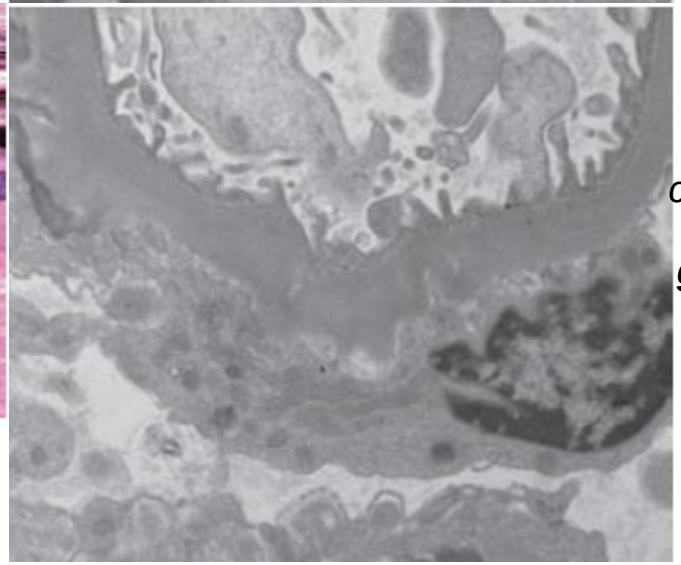
in a patient with metabolic syndrome despite no diabetes

Souraty, Nat.Clin.Pract.Nephrol.(2008) 4:639

PAS methenamine silver stain x400



*selective **capillary** - BM thickening (570nm)*



*control without thickening of **glomerul**.BM (Tungstic acid stain)*

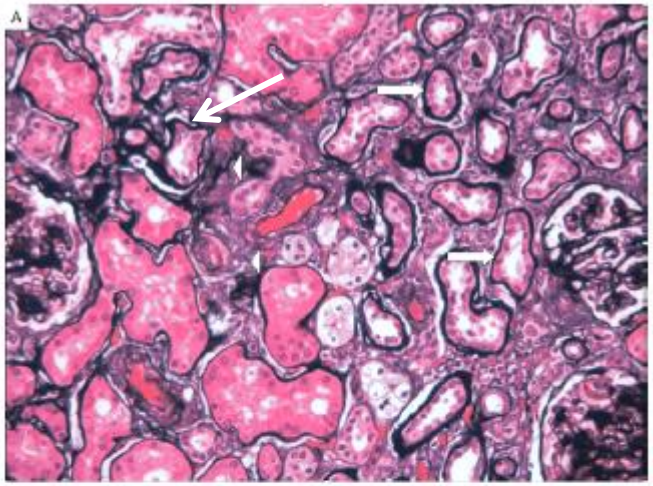
Not only glomerulus

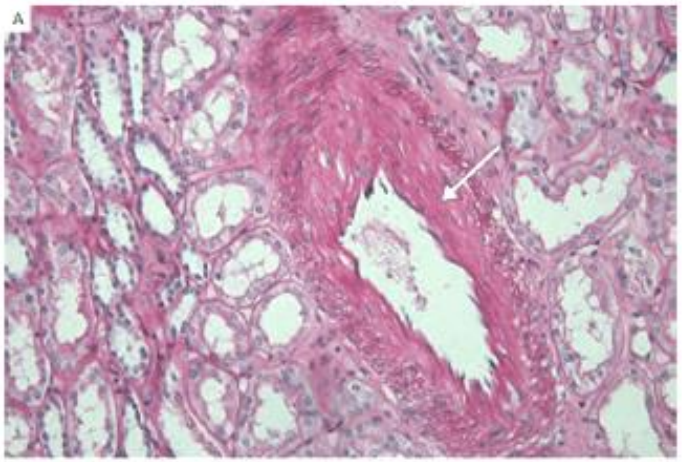
Interstitial fibrosis; tubular atrophy

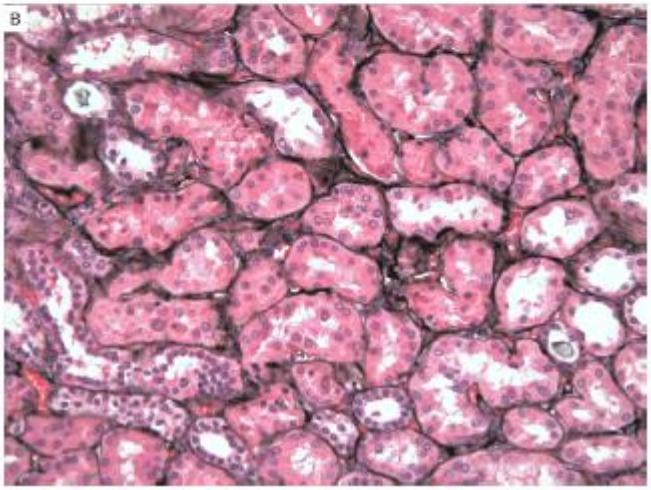
Arterial wall sclerosis *(arrow)*

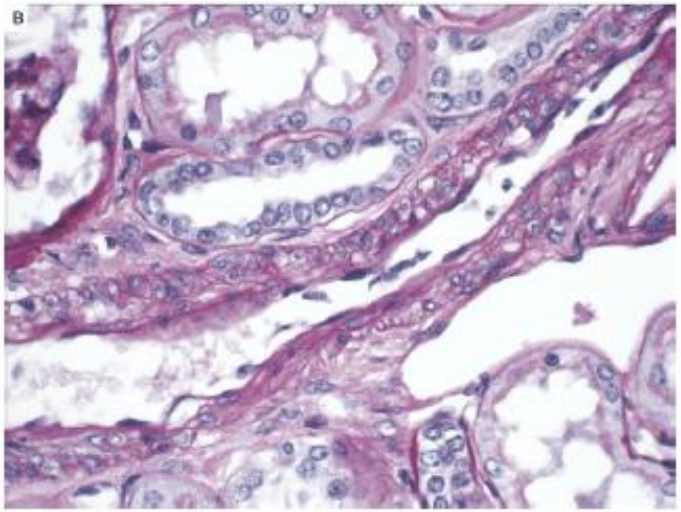
metabolic syndrome

no metabolic syndrome







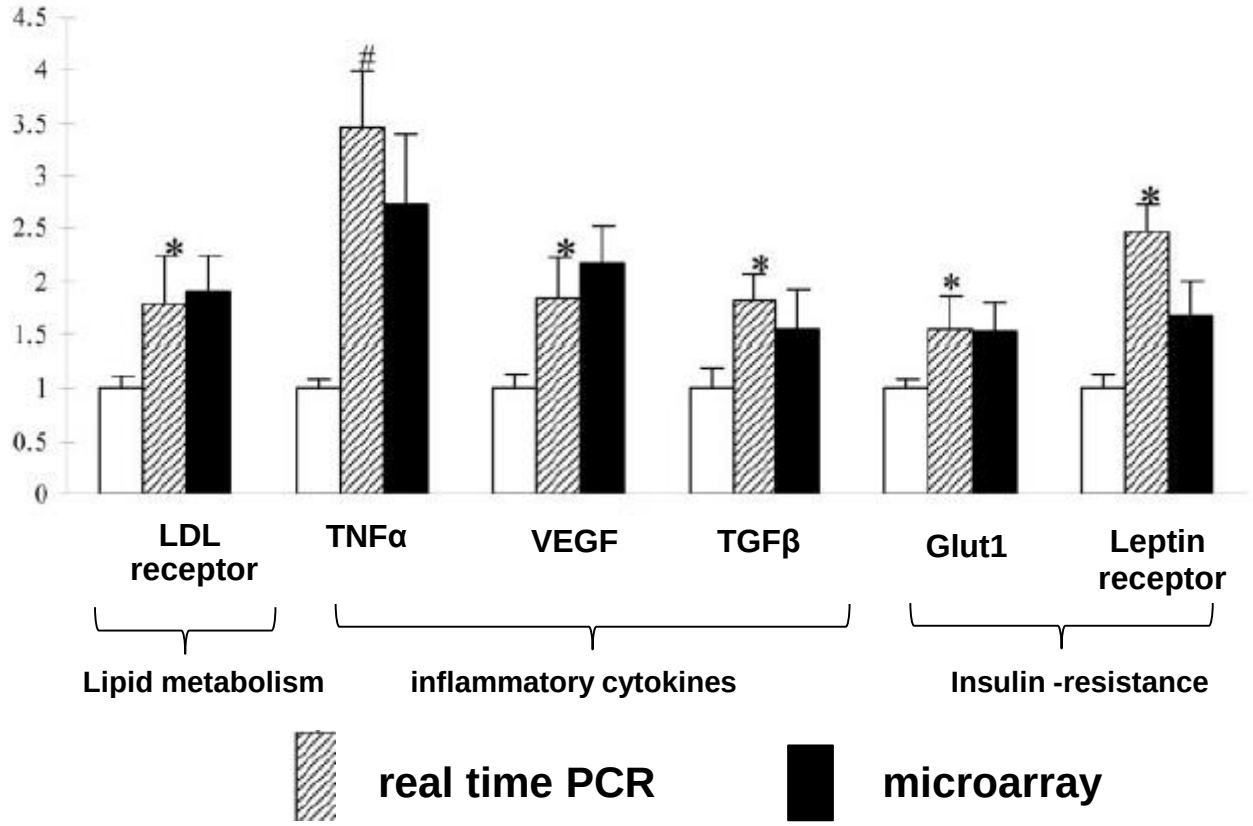


Alexander M. et al
Kidney pathological changes in metabolic syndrome
Am.J.Kidn.Dis.(2009) 53:751

Which biochemical mechanisms involved in obesity associated glomerulopathy ?

glomerular gene expression (microarry and real time PCR)
molecules of lipid metabolism, inflammation, insulin resistance

rel.ratio
(verglichen mit Kontrollen)



Wu, Endocrinology (2006) 147:44

Obesity : renal sequelae

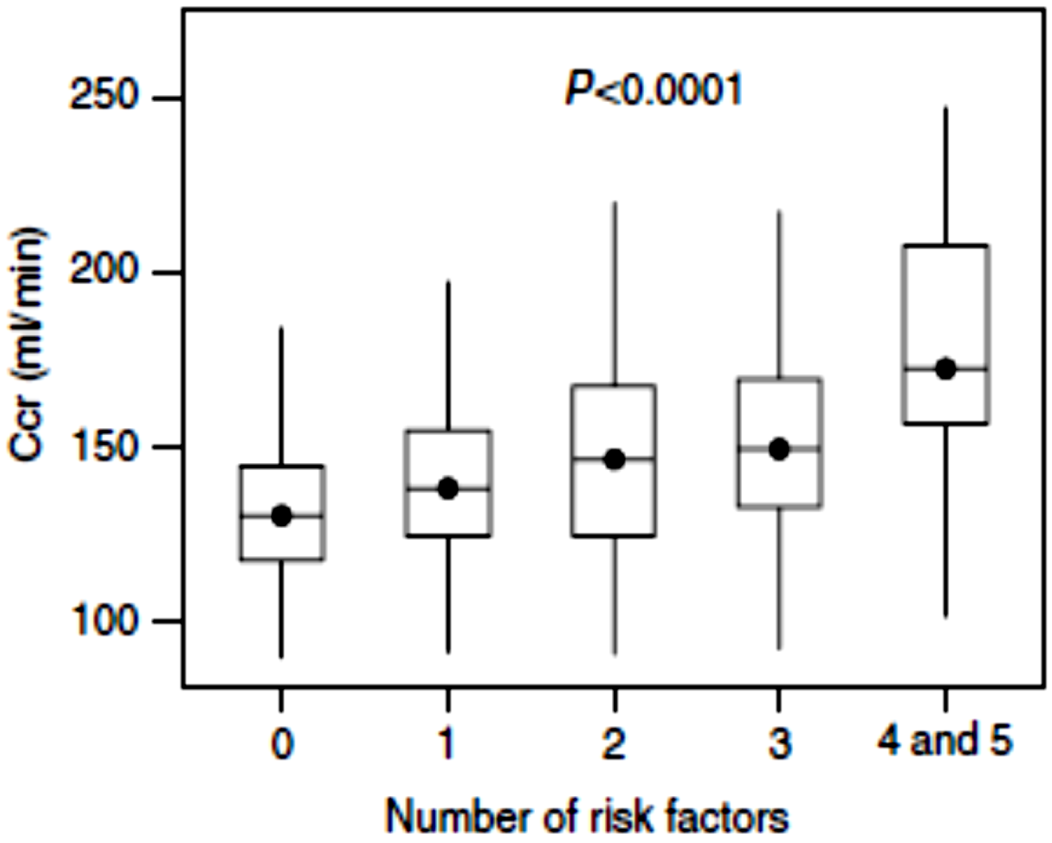
(summary)

- ***Hemodynamics***
  - *increased RPF, GFR, FF, albuminuria*
- ***Structural changes***
  - *increased kidney weight, higher glomerular-volume, mesangial expansion podocyte damage*
- ***Pathology***
  - *glomerulomegaly, glomerulosclerosis, obesity-glomerulopathy*
- ***Chronic kidney disease (CKD)***
  - *proteinuria, increased risk of CKD, progression of CKD*
- ***Terminal renal failure***
  - *increased incidence and prevalence of renal failure, but better survival on dialysis (!),*
  - *increased risk of loss of kidney graft*
- ***Further renal complications***
  - *increased frequency of renal-cell carcinoma and of nephrolithiasis*

Eknoyan, Revista Nefrologia (2011) 31: 397

Metabolic syndrome

hyperfiltration even in young individuals

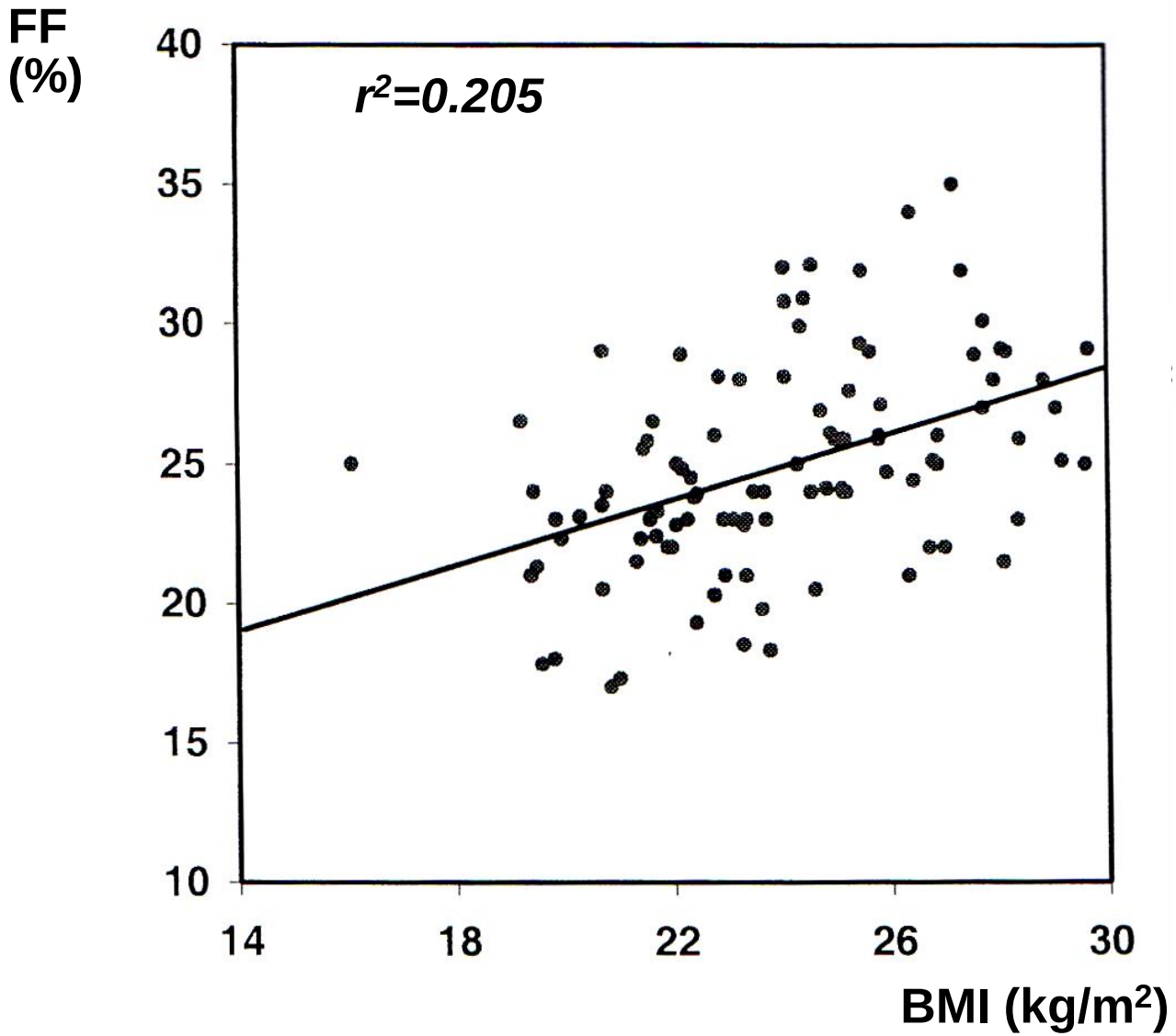


1572 healthy young males (mean age 18 years)

*Risk of hyperfiltration (Cockcroft-Gault Ccr >2SD above mean) → **6.9 fold increased***

Tomaszewski, Kidn.Intern.(2007) 71:816

Correlation between BMI and filtration fraction (FF) *presumably indicating glomerular hypertension*

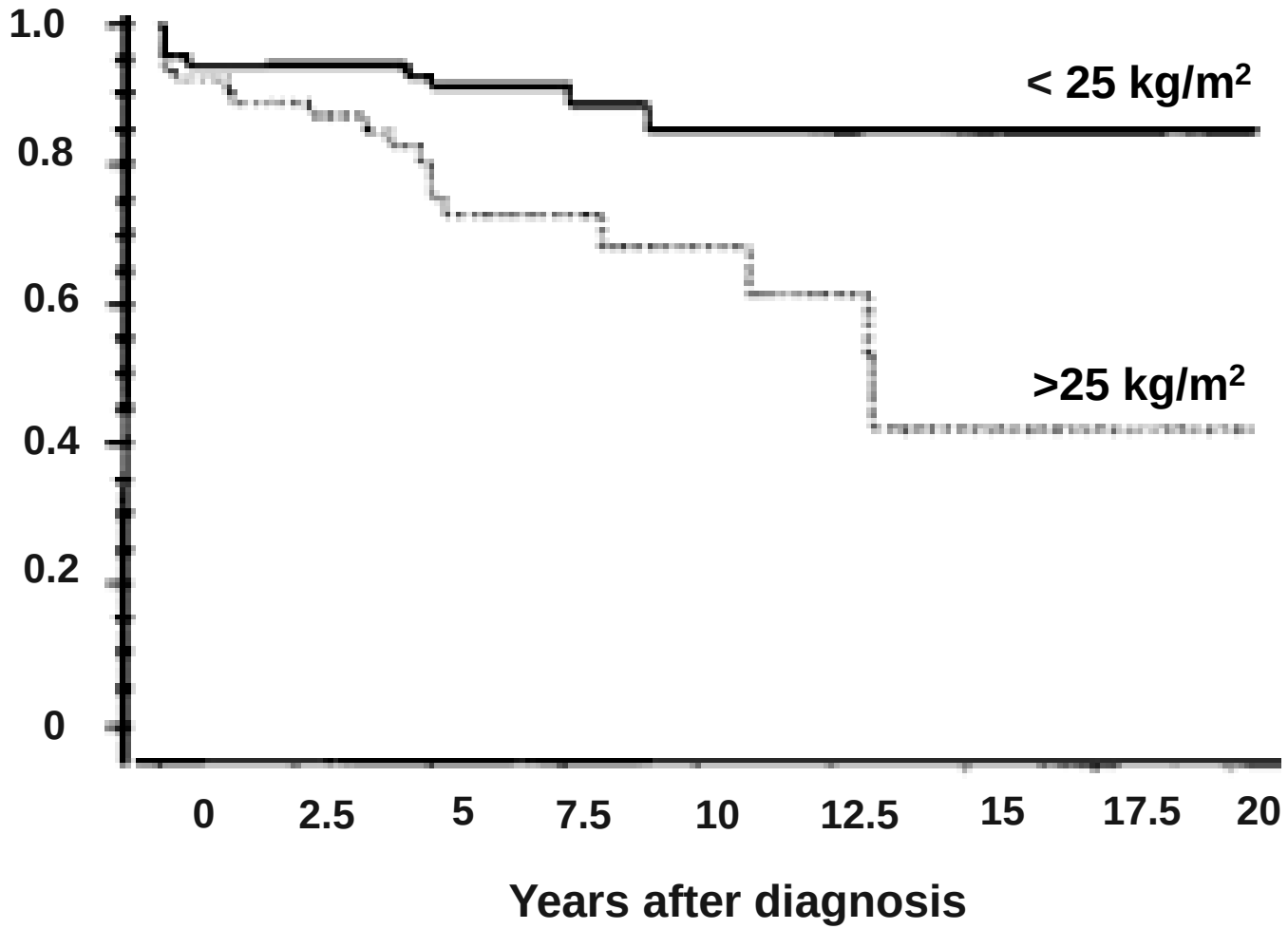


Bosma, Kidn.Internat.(2004) 65:259

Patients with IgA-GN

(as <u>one</u> example of primary kidney disease)

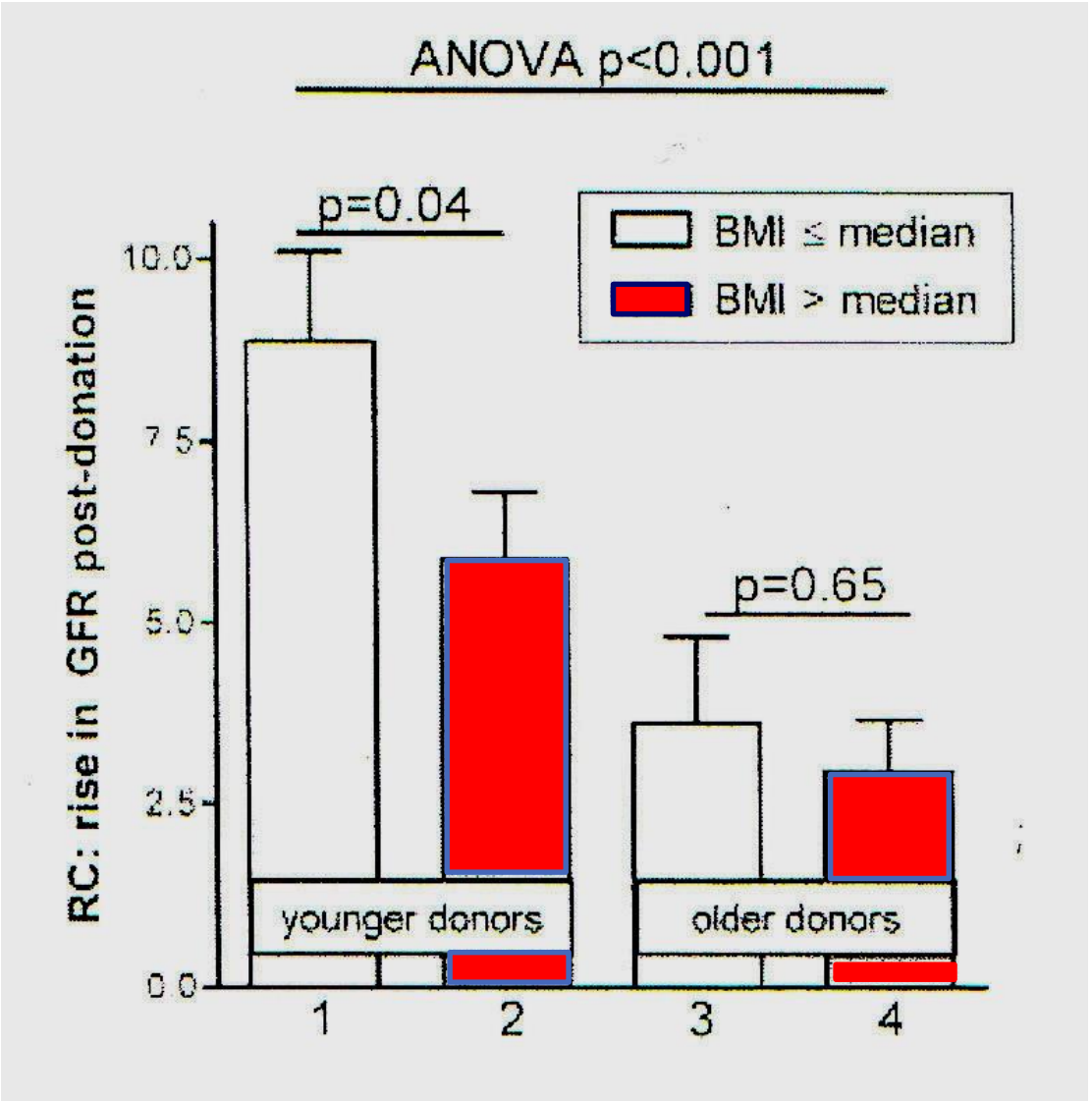
Onset of CKD dependent on BMI



Bonnet, Am.J.Kidn.Dis.(2001) 37:720

In individuals with advanced age
high BMI ⇨ glomerular reserve reduced *(kidney donors)*

glomerular reserve:
Δ GFR after Dopamin



Bosma, Am.J.Transpl. (2008) 8:2077

Estimation of GFR :

Obesity increases Cystatin C values independent of GFR

Cystatin C *(endogenous Cathepsin Protease Inhibitor)*

in obesity increased production by human adipocytes in vitro

Comparison :

237 individuals without obesity (age 51 years; BMI 22.8±0.11kg/m^2)

248 individuals with obesity (age 50 years; BMI 34.7±0.29kg/m^2)

Cystatin C serum concentration increased in obesity of both genders

– independent of GFR

fat tissue biopsies :

gene expression and secretion of Cystatin C increased

(subcutaneous and omentum fat)

Naour, Obesity (Silver Spring) (2009) 17:2121

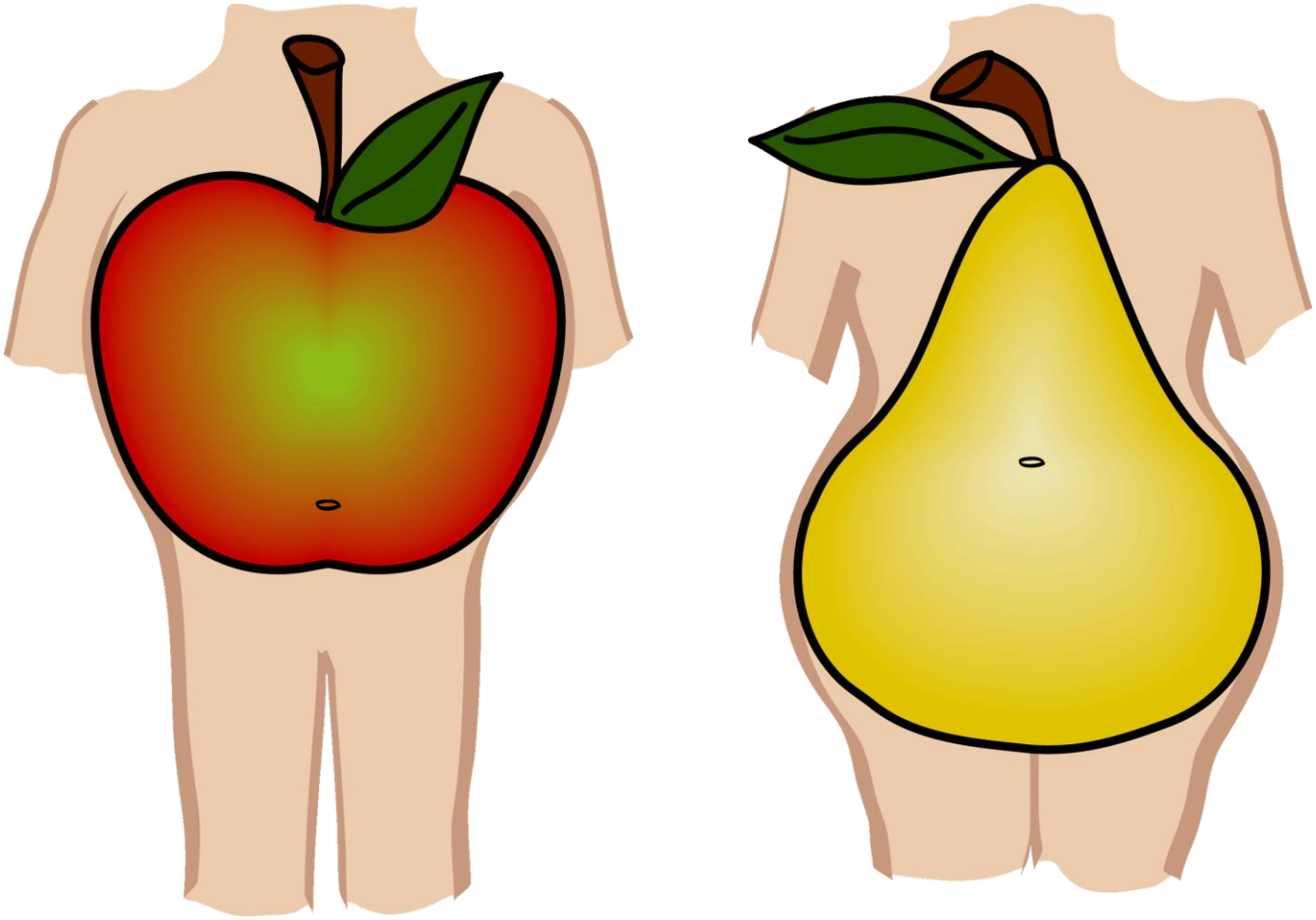
Obesity and the kidney

Venus of Willendorf (Austria) 4000 BC

- **Epidemiology of CKD and ESRD in obesity**
- **Renal morphology and function in obesity**
- **Role of visceral obesity**
- **Reversibility of renaL pathology in obesity**
- **Renal consequences of bariatric surgery**
- **“Obesity” – always detrimental ?**
  (“one body weight is optimal for all?”)


Waist circumference
♂ 102 cm, ♀ 88 cm

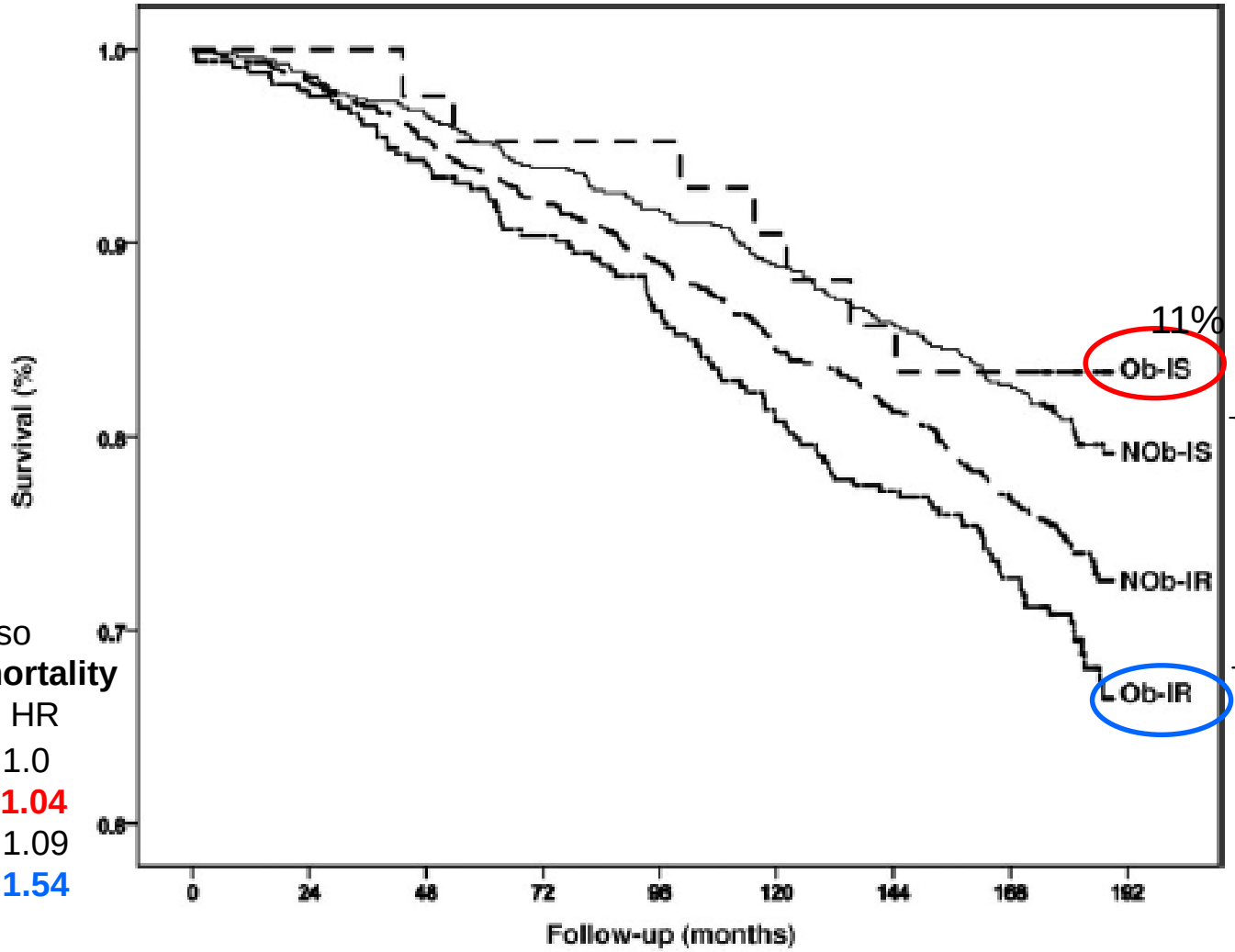
Android (apple) vs.gynoid (pear) obesity



A pioneer: Jean Vague, Marseille (1947)

Mortality *(incl. carcinoma-mortality)* **not increased in obese individuals with normal insulin sensitivity**

(Cremona study)



obese
insulin sensitive
not obese

obese
insulin resistant
obese

lower also **carcinoma mortality**

	HR
non-obese IS	1.0
obese IS	**1.04**
nonobese IR	1.09
obese IR	**1.54**

not all obese are at risk , only the ones with insulin resistance

Calori, Diabetes Care (2011) 34:210

Visceral obesity and kidney function

("normal weight obesity")

even in individuals with normal body mass index (BMI)
central fat deposition (waist-hip ratio) is associated with

higher rik of :

 # microalbuminuria

RR 1.7 *(1.19-3.12)*

 # reduced eGFR

RR 1.9	*(1.19-3.12)*	***"lean"***
2.0	*(1.19-31.9)*	***"overweight"***
2.7	*(1.46-4.85)*	***"obese"***

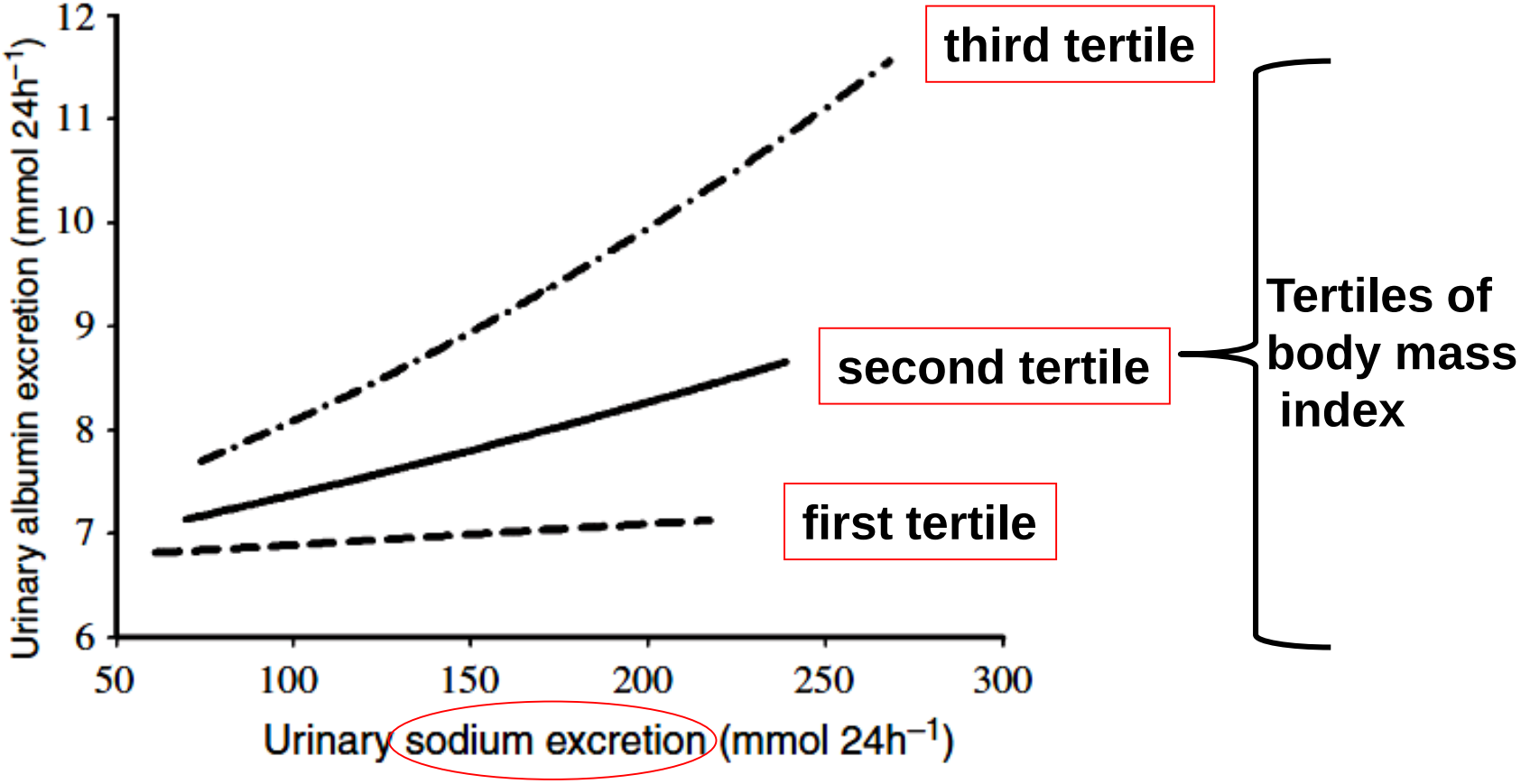
Pinto-Sietsma, Am.J.Kidn.Dis.(2003) 41: 733

The higher the "body mass index" *the more albumin excretion is amplified -*

but this is further amplified by high NaCl intake

(Prevend study)

Albuminuria



Verhave, J.Intern.Med.(2004) 256:324

The Paradox of Insulin-Resistance

- **Insulin sensitivity is reduced in:**

✓ *Muscle*
✓ *Fat tissue*
✓ *Liver*
✓ *...*

- **but Insulin sensitivity is not reduced in :**

the Kidney → ***increased sodium reabsorption***

Rocchini, Hypertension (1989) 14:367

the CNS → ***increased sympathetic-tone***

Landsberg, J.Hypertens. (2001) 19:523

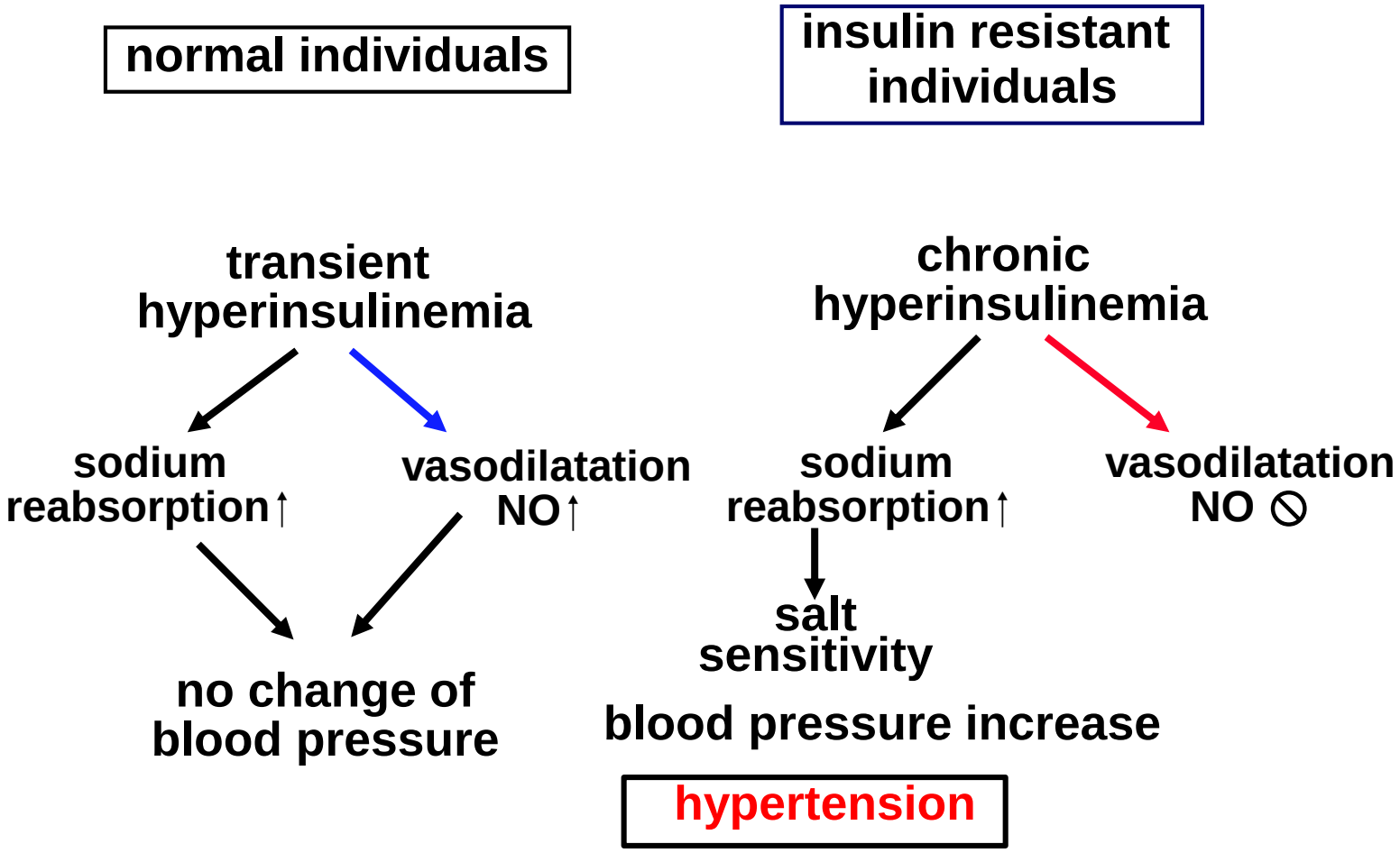
Patients with metabolic syndrome
⇩ increased blood pressure response to salt intake

Metabolic syndrome components	Blood pressure-decrease switch from 8.2 → 2.3 g NaCl/day
4-5	- 8.7 ± 1.3 mmHg
3	- 6.0 ± 1.1 mmHg
< 3	0 mmHg

p<0.0001

Hoffmann, J.Human Hypertens.(2007) 21:438

Why does sodium intake increase blood pressure preferentially in insulin resistance?



→ ***antinatriuretic effect of insulin maintained***
→ ***vasodilatory NO mediated effects are cancelled***
→ ***RAS upregulated***

after Bakris,

Adiposity

RAS

- activated

Gorzelniak,J.Hypertens.(2002) 20:965

Aldosteron-secretion

- **independent of classical stimuli aldosterone synthesis stimulated by a factor synthesized in visceral fat cells**

(adipocyte derived secretagogue EKODE, produced in visceral adipocytes)
Erhart-Bornstein, Proc.Natl.Acad.Sci USA (2003) 100:1421
Goodfriend Hypertension (2004) 43:358

Aldosteron novel treatment target in visceral adiposity

- Factor produced in visceral fat cells stimulates aldosteron synthesis causing aldosteron-produced podocyte-damage

  (rat model of metabolic syndrome)

Nagase, J.Am.Soc.Nephrol.(2006) 17:3438

- Eplerenone → reduction of podocyte-damage and proteinuria

Nagase, Hypertension (2006) 47:1084

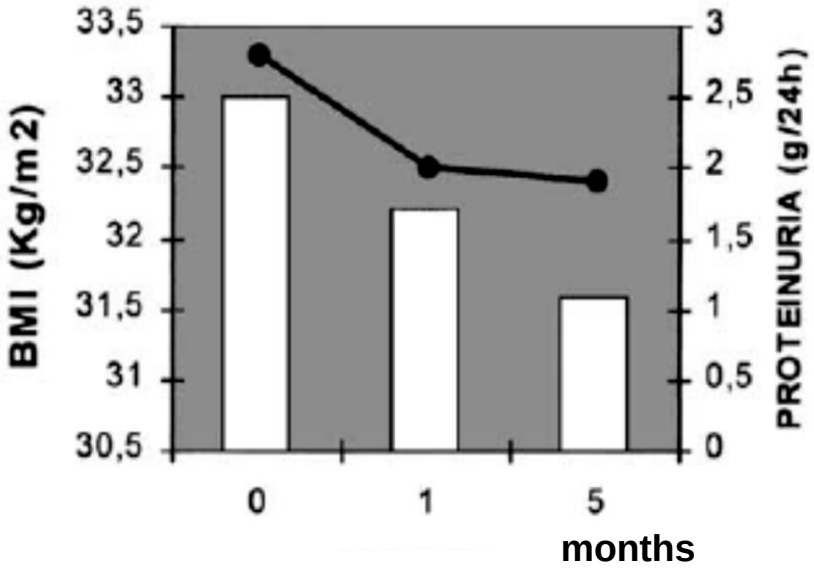
Obesity and the kidney

Venus of Willendorf (Austria) 4000 BC

- **Epidemiology of CKD and ESRD in obesity**
- **Renal morphology and function in obesity**
- **Role of visceral obesity**
- **Reversibility of renal pathology in obesity**
- **“Obesity” – always detrimental ?**
  (“one body weight is optimal for all?”)

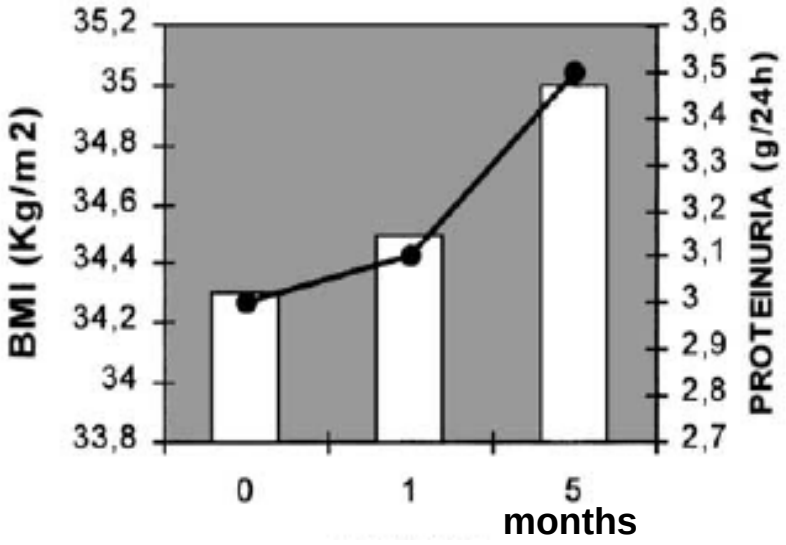
Weight loss and reduction of **Proteinuria**

(prospective controlled study)



intensified treatment

(weight loss)

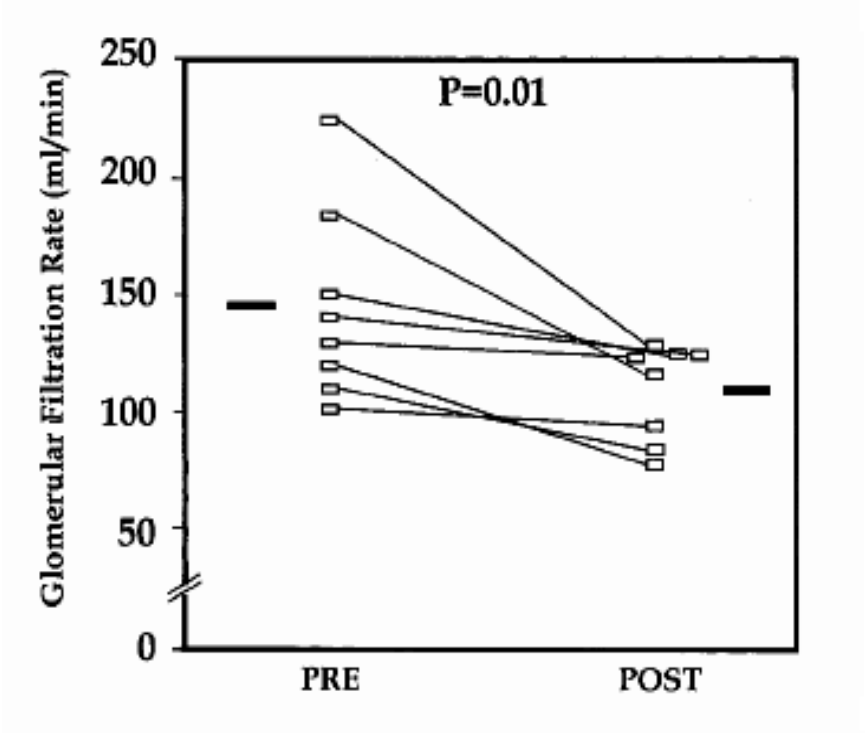


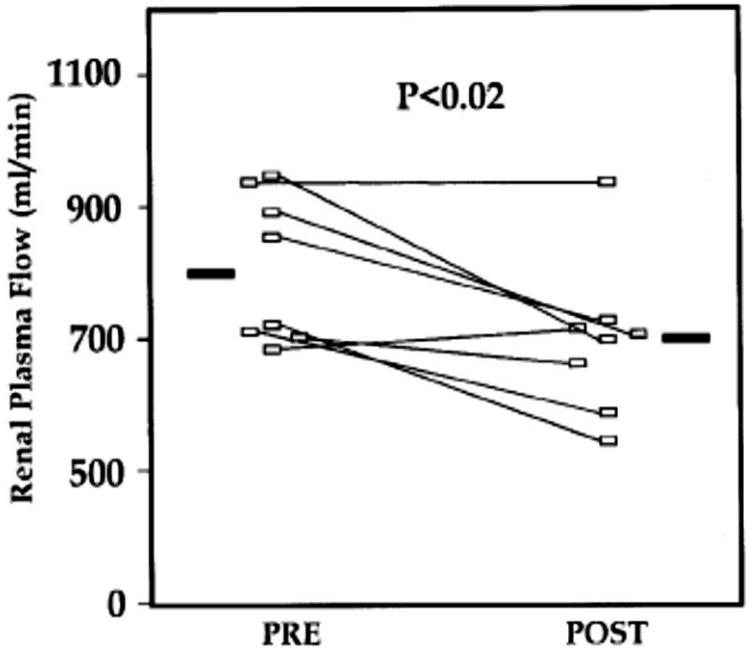
routine treatment

Morales, Am.J.Kidn.Dis.(2003) 41:319

Weight reduction in morbid obesity → regression of GFR, RPF and Albuminuria

BMI 48±2.4 → 32.7±1.5 kg/m2





Albuminuria from 16 µg/min (4-152) to 5 µg/min (3-37)

Chagnac, J.Am.Soc.Nephrol.(2003) 14:1480

Impact of body weight reduction on renal function in CKD patients

38 obese CKD patients

2 months; reduction of body weight >3%

s-creatinine	**1,1**±*0.3*	→ **0.8**± *0.3*	*p<.001*
eGFR	**75.9**±*21.2*	→ **104**± *50.0*	*p<0.001*
proteinuria	**73%**	→ **50.5%**	*p=0.02*

Wang, J.Renal Nutrition (2013) e-pub Jun 2013)

Obesity and the kidney

Venus of Willendorf (Austria) 4000 BC

- **Epidemiology of CKD and ESRD in obesity**
- **Renal morphology and function in obesity**
- **Role of visceral obesity**
- **Reversibility of renaL pathology in obesity**
- **Renal consequences of bariatric surgery**
- **“Obesity” – always detrimental ?**
  (“one body weight is optimal for all?”)

Bariatric surgery – stop and reversal of progression of CKD

25 patients CKD 3 (GFR 30-59 ml/min/1.73m^2)
“morbid obesity“ (BMI 49.8 kg)
GFR 47.9 ml/min/1.73m^2)

1 year after surgery control :

body mass index :
from 49.8 to 34.5 kg/m^2

systolic blood pressure :
from 133±13 mmHg to 128±17 mmHg

eGFR :
from 47.9 to 61.6 ml/Min/1.73m^2

Navaneethan, Surg.Obes.Relat.Dis.(2009) 5:669

But no improvement of survival ?

Retrospevtive Cohort study VA 2000 - 2006
850 Veterans compared to 41,244 non-operated controls
mean age 49,5 years, BMI 47,4 ± 7,8
6.7 years follow-up

Non-adjusted Cox regression analysis :

reduction of mortality **HR 0.64** *(CI 0.51 - 0.8)*

"Propensity matched" analysis

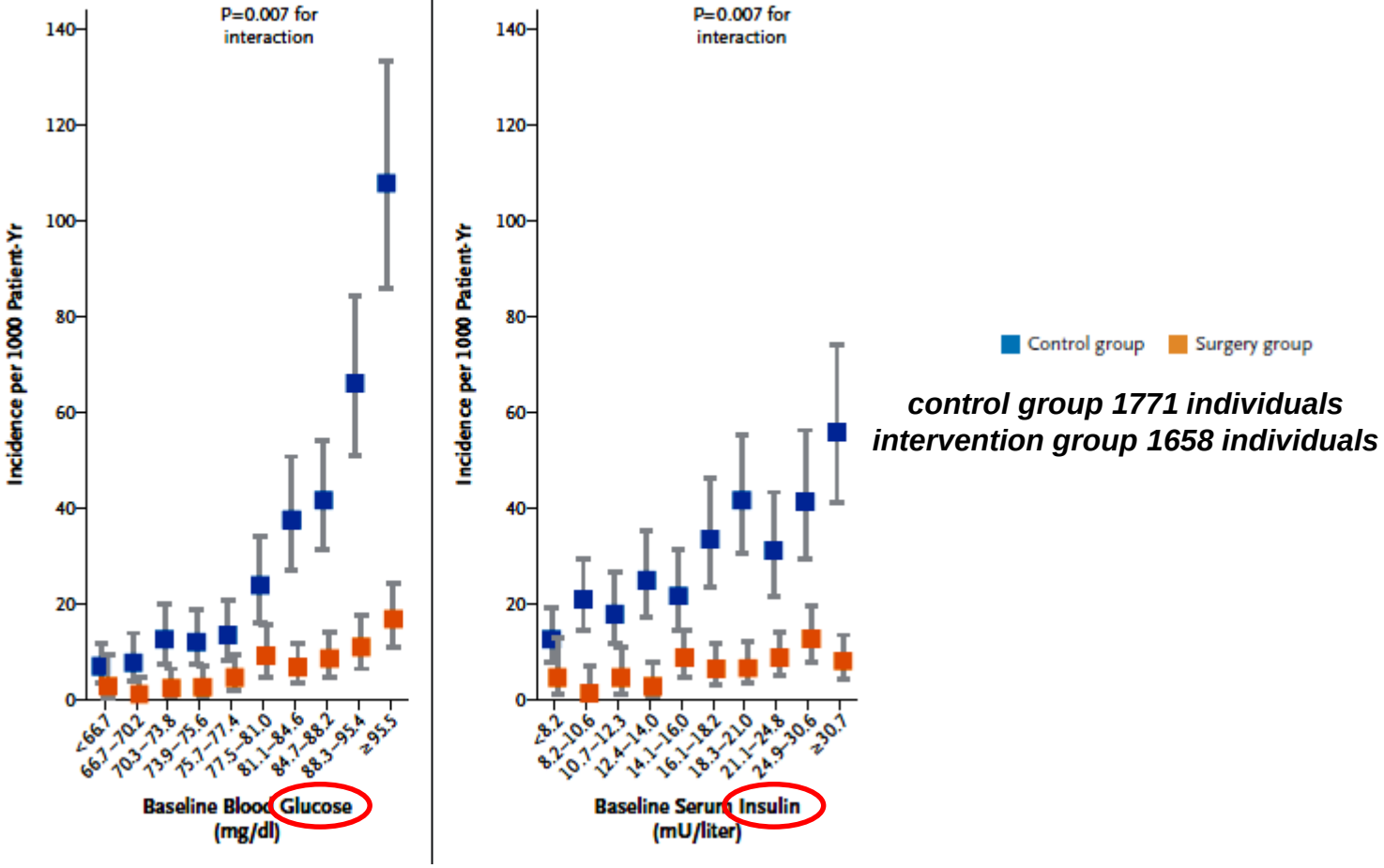
no significant reduction of mortality **HR 0.83** *(CI 0.61 - 1.14)*

Maciejewski, JAMA (2011) 305: 2419

Bariatric Surgery : Prevention of Type 2 Diabetes

(SOS study [Swedish obese subjects])

15 years study, onset of type 2 diabetes in individuals with elevated basal-glycemia and basal insulin concentration



control group 1771 individuals
intervention group 1658 individuals

Carlsson, New Engl.J.Med.(2012) 367: 695

Obesity and the kidney

Venus of Willendorf (Austria) 4000 BC

- **Epidemiology of CKD and ESRD in obesity**
- **Renal morphology and function in obesity**
- **Role of visceral obesity**
- **Reversibility of renal pathology in obesity**

Obesity

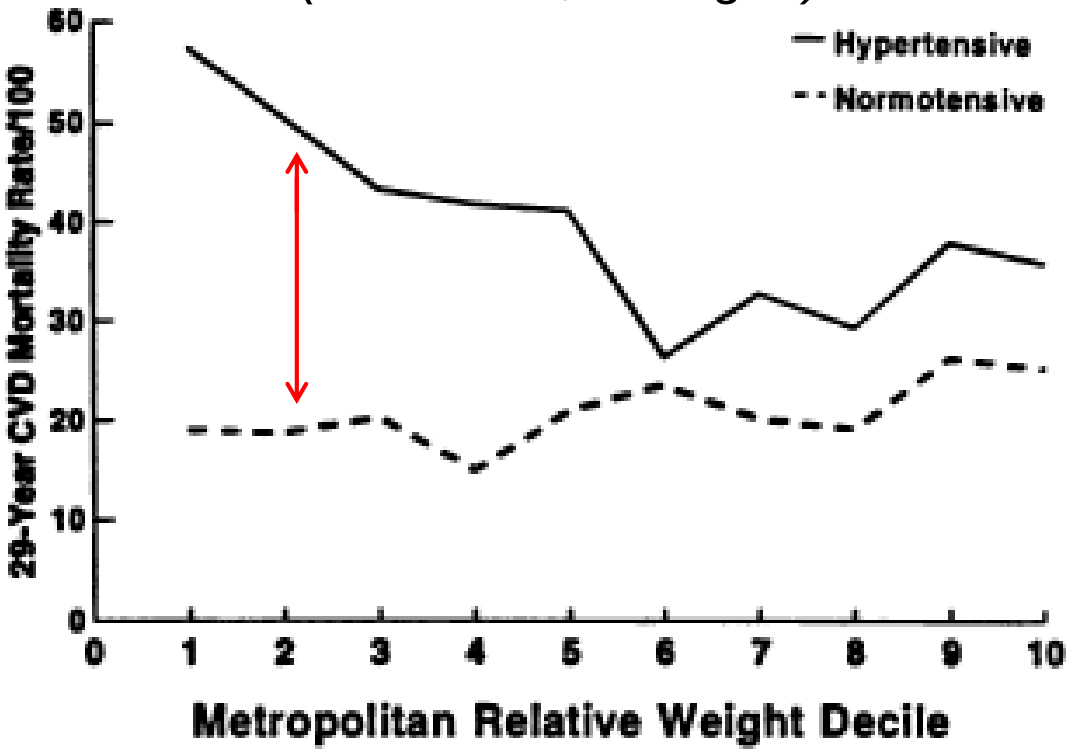
- *not simply high body weight .*
- *the type of fat*
- *the distribution of fat deposits …*

- **“Obesity” – always detrimental ?**

(“is one body weight: optimal for all?”)

Cardiovascular mortality is higher in meager individuals with hypertension

(Tecumseh, Michigan)



Graph of age-adjusted 29-year cardiovascular disease (CVD) mortality by decile of Metropolitan relative weight and hypertension status.

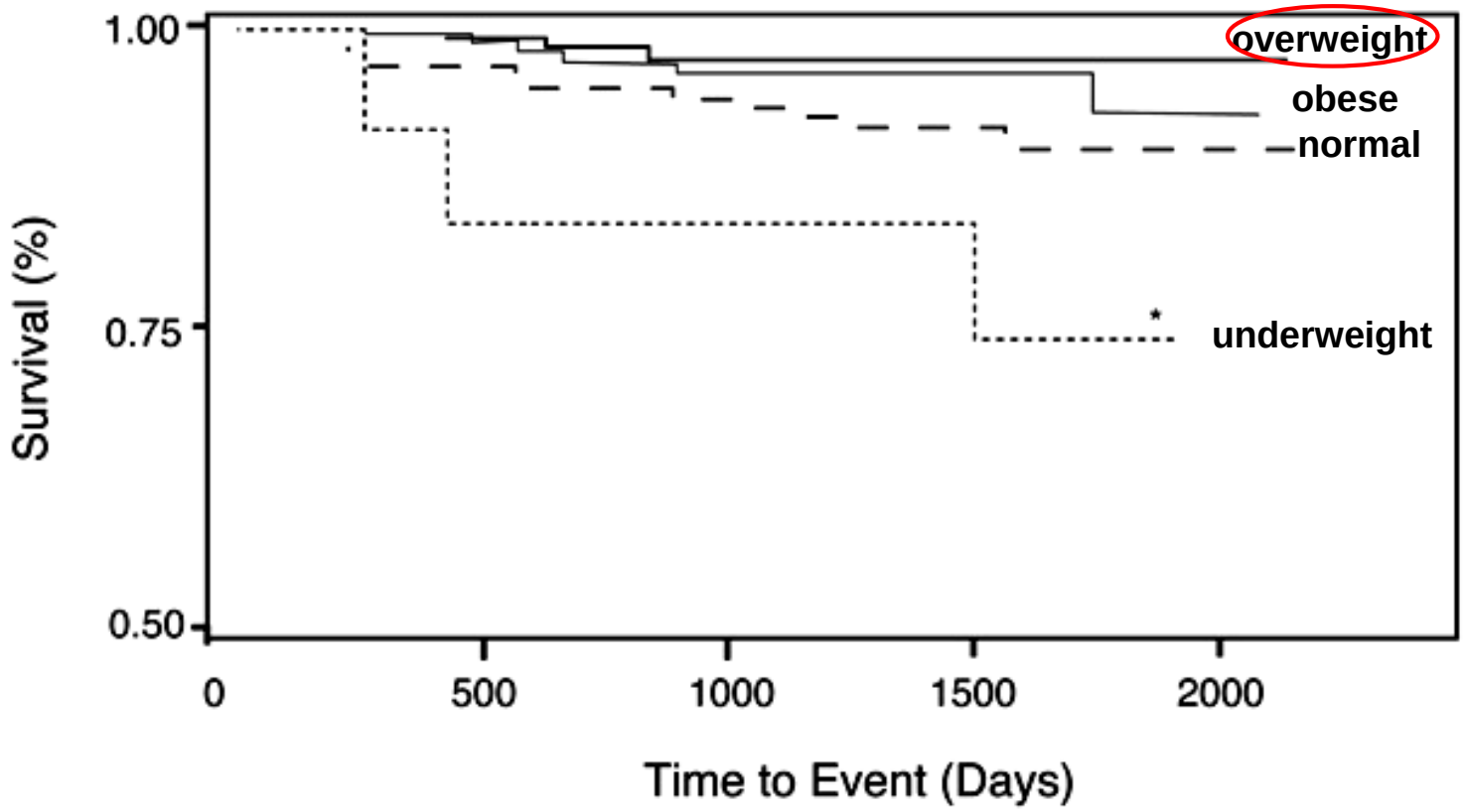
Carman, Circulation (1994) 89:703

⇨ **meager individuals : more frequently hypertensive and higher reactivity of neuroendocrine systems (sympathetic and RAS systems)**

Weber, Lancet (2013) 381:537

“Obesity paradox“

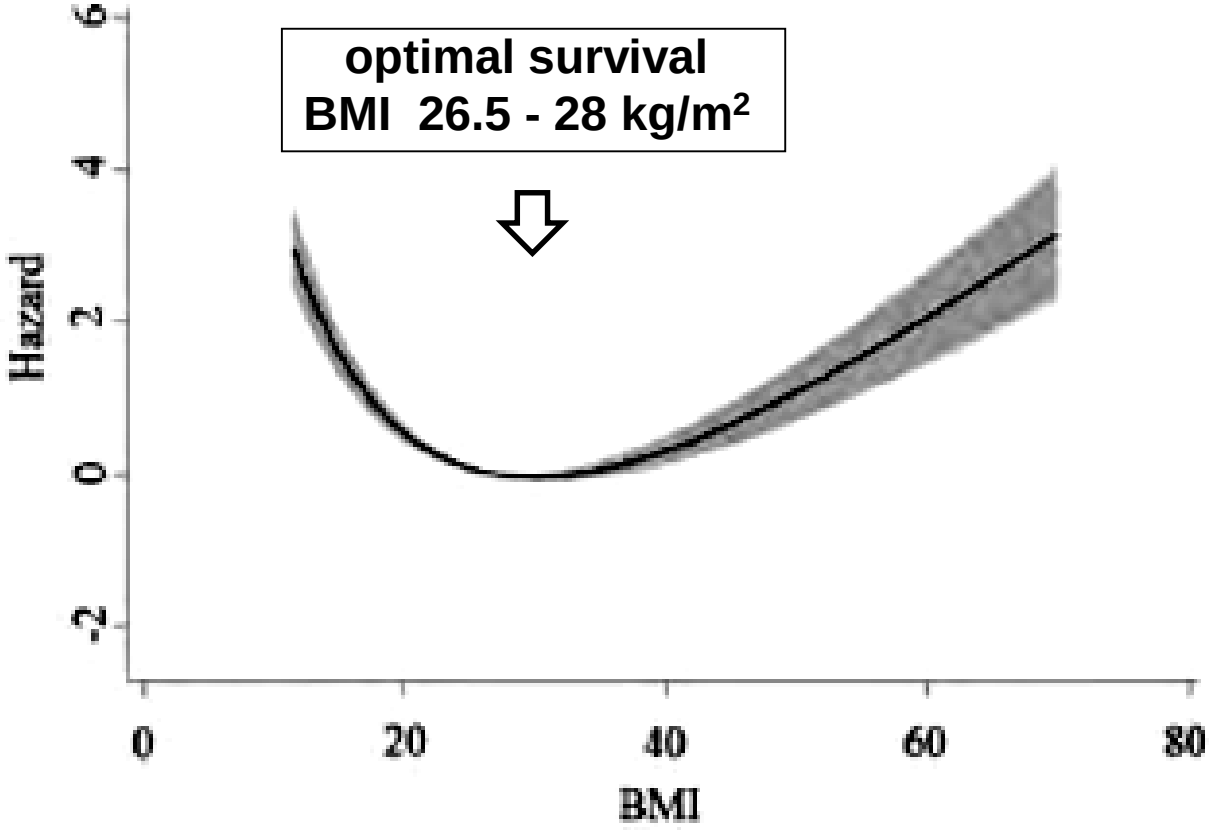
571 patients with stable coronary heart disease
highest event rate in underweight patients
best outcomes in overweight patients without obesity



DeSchutter, J.Am.Coll.Cardiol.(2011) 57:E570

BMI and “all-cause“ mortality

Patients with acute coronary syndrome and/or significant coronary heart disease



Angerås, Europ.Heart J.(2013) 34:345

Obesity and Kidney

Venus von Willendorf 4000 BC

- **Epidemiology of obesity**
- **Epidemiology of CKD and ESRD in obesity**
- **Renal morphology and function in obesity**
- **The role of visceral obesity**
- **Reversibility of renal morphology and function in obesity**
- **Renal outcomes after bariatric surgery**
- **“Obesity“ – always detrimental ?**
  (“one single weight is not optimal for all“)

Thank you for your attention

prof.e.ritz@t-online.de

Obesity and the kidney

Venus of Willendorf (Austria) 4000 BC

- **Epidemiology of CKD and ESRD in obesity**
- **Renal morphology and function in obesity**
- **Role of visceral obesity**
- **Reversibility of renal pathology in obesity**

Obesity

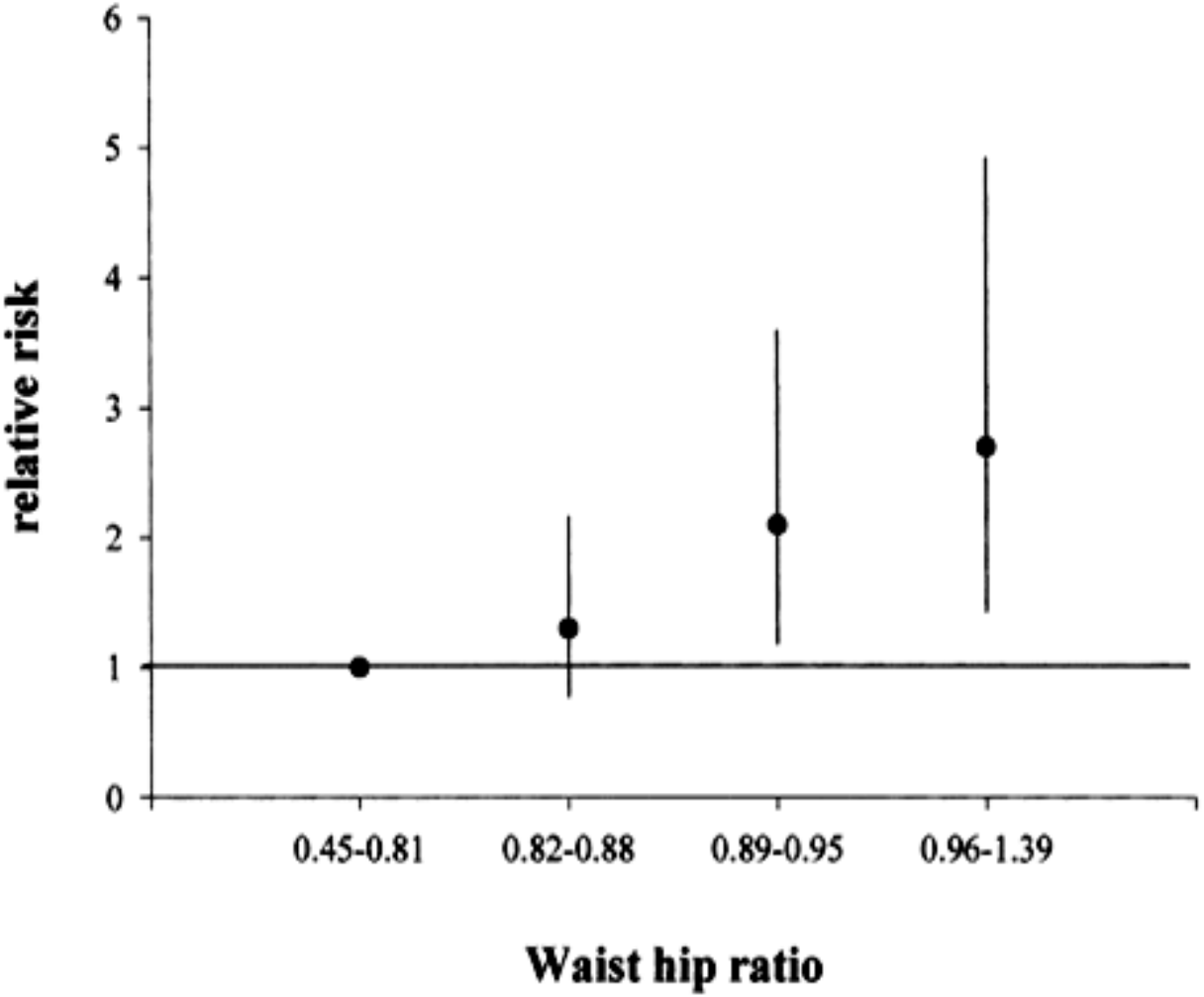
- *not simply high body weight .*
- *the type of fat*
- *the distribution of fat deposits …*

- **“Obesity” – always detrimental ?**

(“is one body weight: optimal for all?”)

Even in the general population the relative risk of eGFR loss depends on waist-hip ratio

PREVEND study (Groningen)



Pinto-Sietsma, Am.J.Kidn.Dis.(2003) 41: 733

Why increased salt sensitivity ?

Increased glomerular filtration in obesity :

⇨ increased proximal tubular sodium reabsorption

Study in 12 obese (BMI > 36) and 19 normal weight individuals :

GFR, **RPF**, **FF**

fractional excretion of lithium *(index of fractional proximal tubular Na reabsorption)*

6 of 12 obese individuals:

⇩

increased GFR and FF,

higher postglomerular oncotic pressure,

increased tubular Na^+ reabsorption,

(low Lithium clearance)

higher glomerular capillary pressure ?

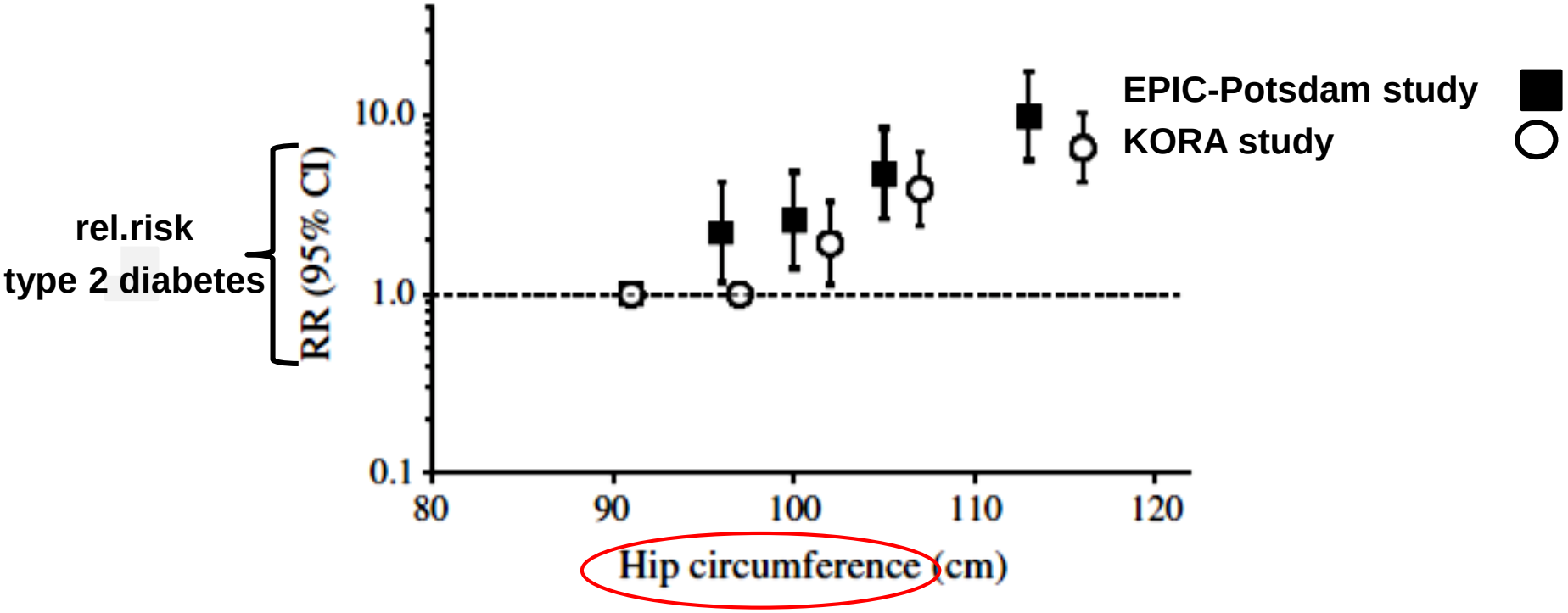
Chagnac, Nephrol.Dial.Transplant.(2008) 23:3946

Assessment of body fat in women

⇨ *"waist circumference"*

***best* predictor of percent body fat**

(validated by magnetic resonance tomography)



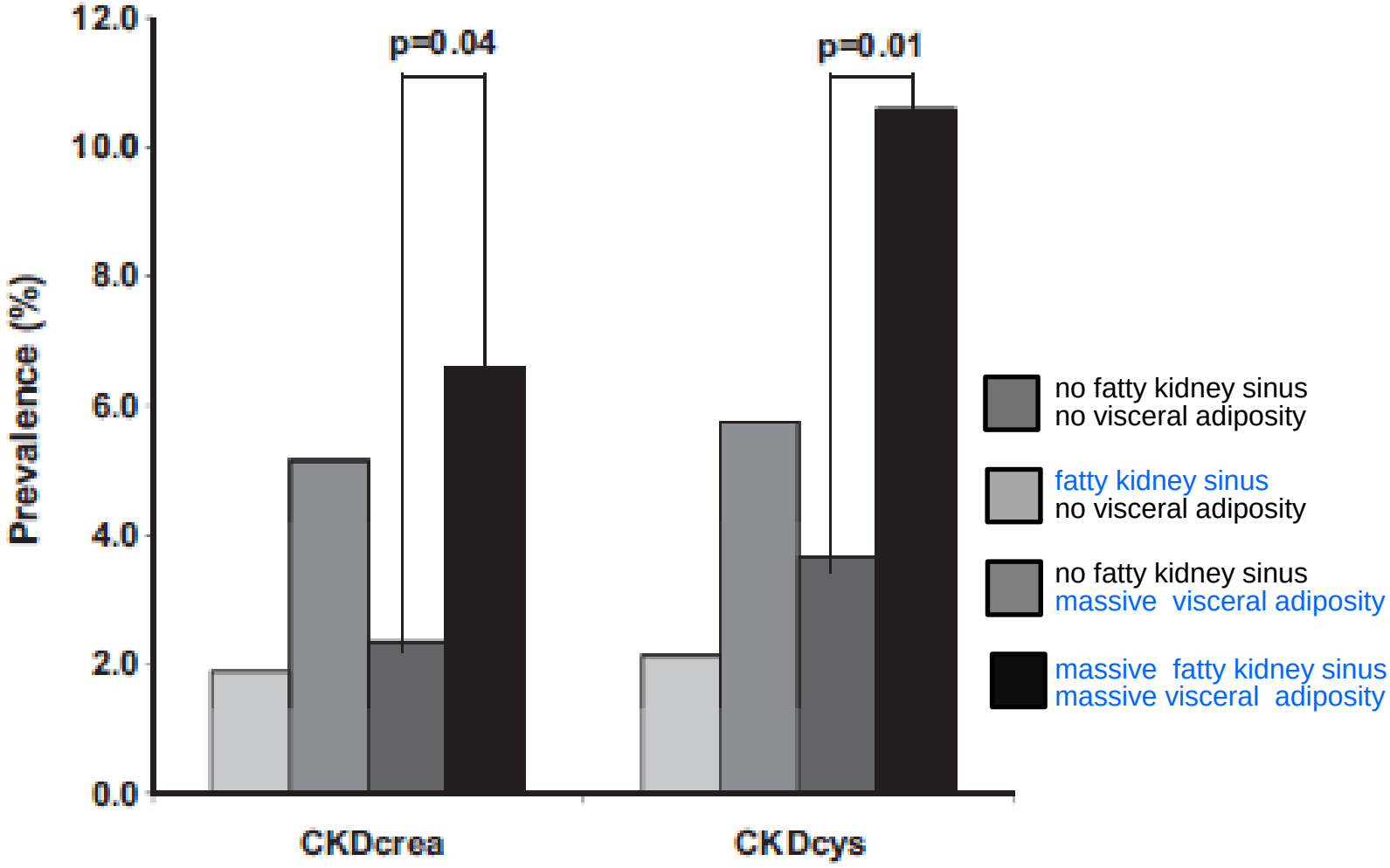
Schulze, Diabetologia (2012) 55:1660

Prevalence of “chronic kidney disease“ (CKD)

(serum creatinine and Cystatin C)

relation to “fatty kidney sinus“ and visceral adiposity

(Framingham Heart Study)

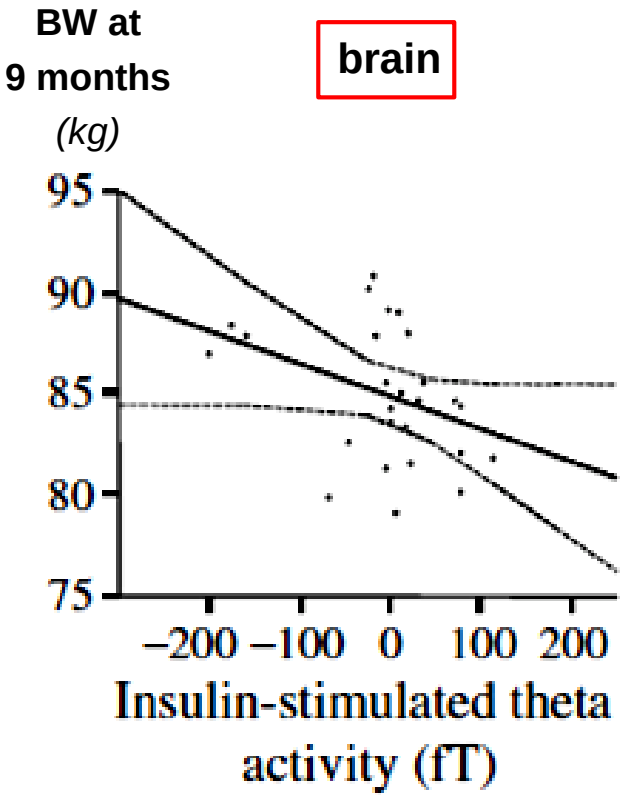


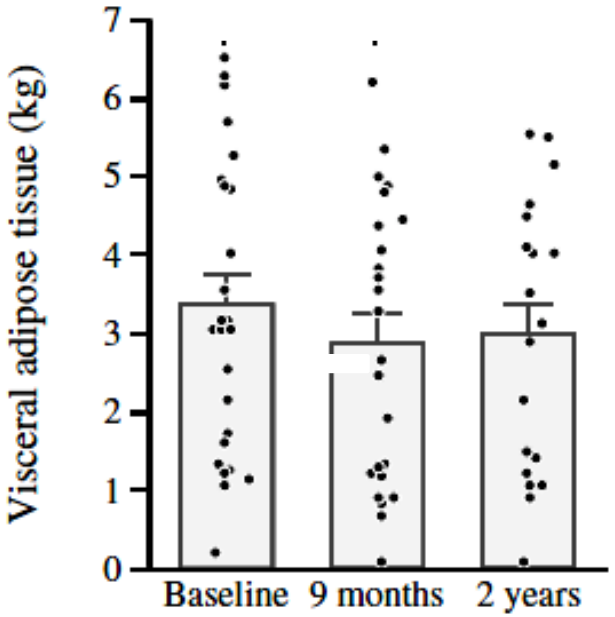
Foster, Hypertension (2011) 58:784

Another culprit : cerebral insulin resistance

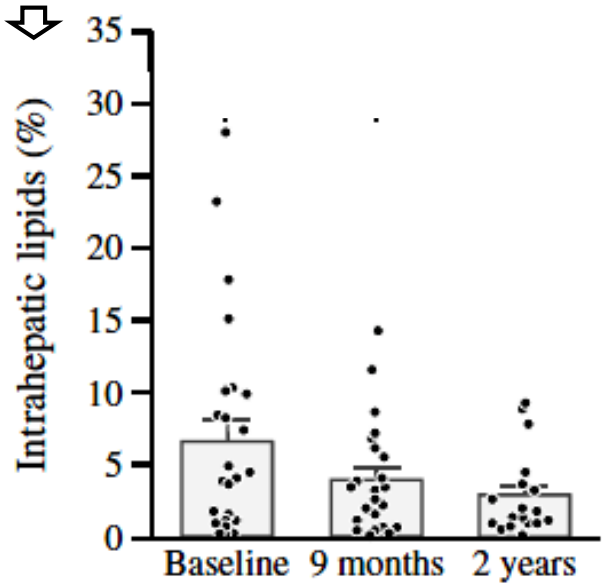
insulin resistance favours increased body weight and body fat (incl. fat in renal pelvis) reversible by "lifestyle intervention"

(Tübingen lifestyle study)





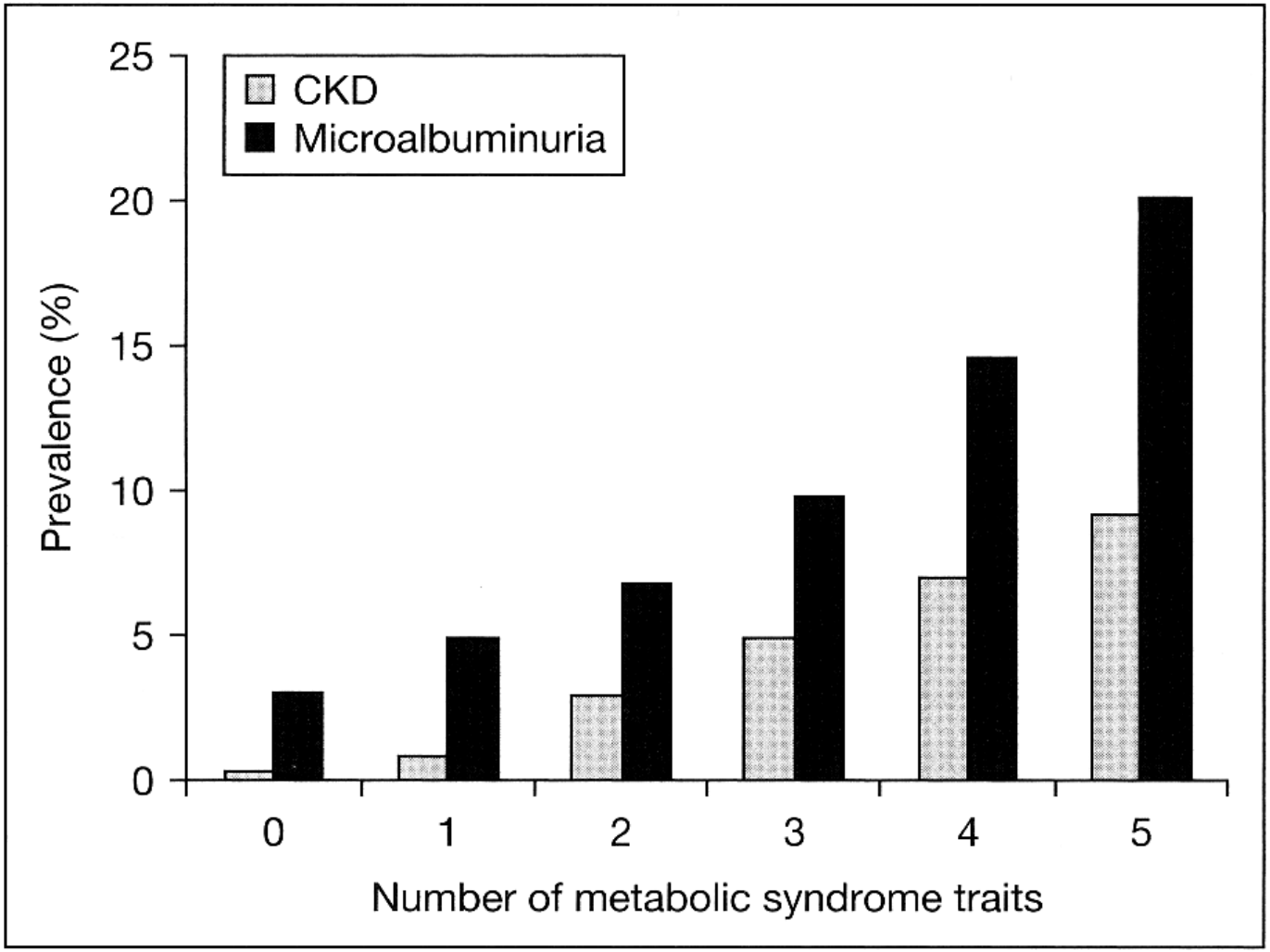
visceral fat



intrahepatic fat

Tschritter, Diabetologia (2012) 55:175

Different severity of the metabolic syndrome and the resulting prevalence of CKD (*chronic kidney disease*) and microalbuminuria

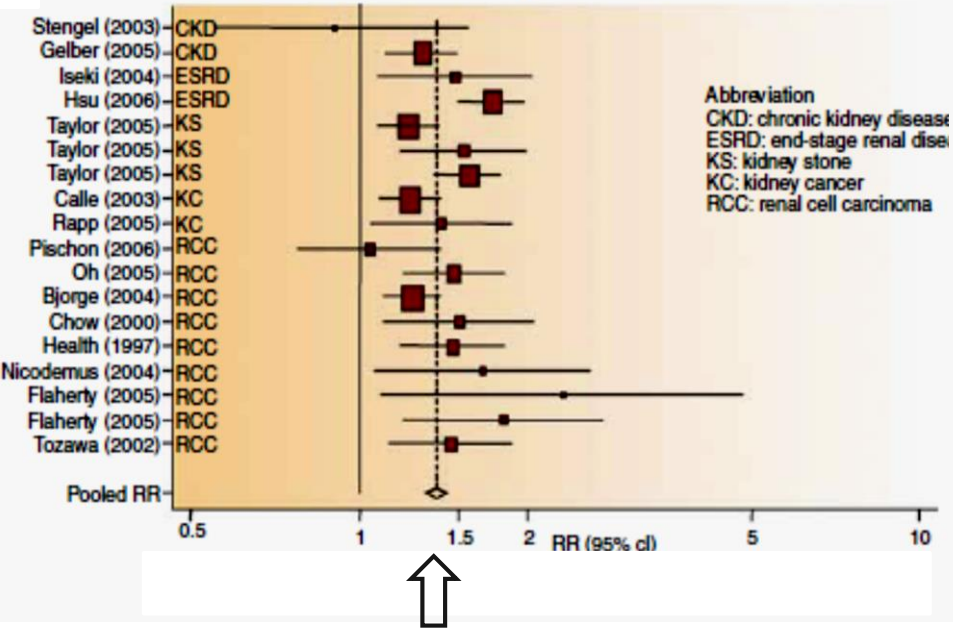


Kramer, Contrib.Nephrol.(2006) 151:1

Body mass index and CKD

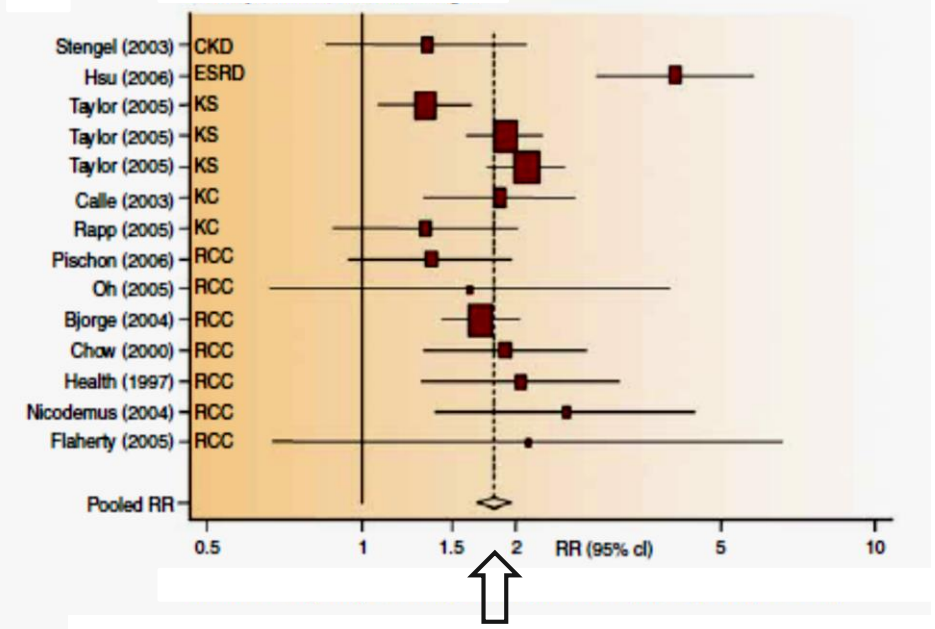
Metaanalysis

Overweight *BMI 25-30 kg/m²*



rel.Risk 1,4

Obesity *BMI >30 kg/m²*

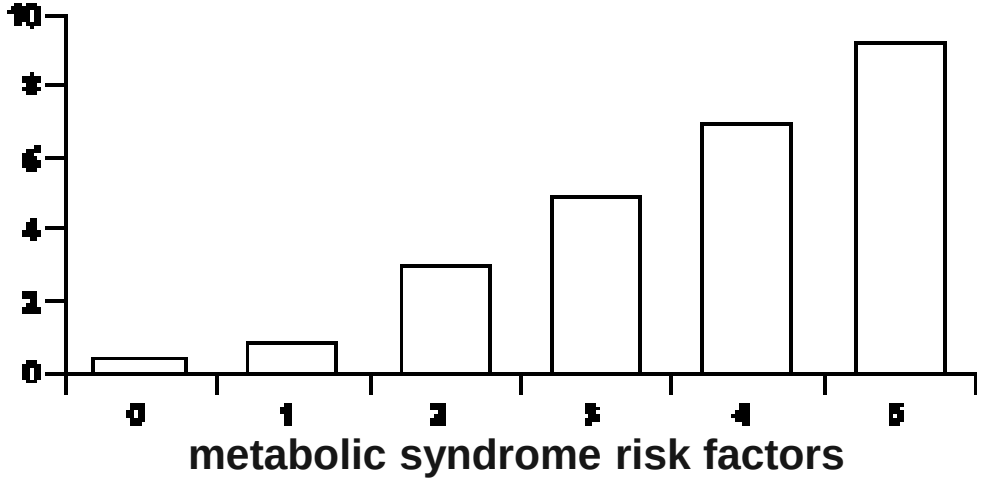


rel.Risk 1,9

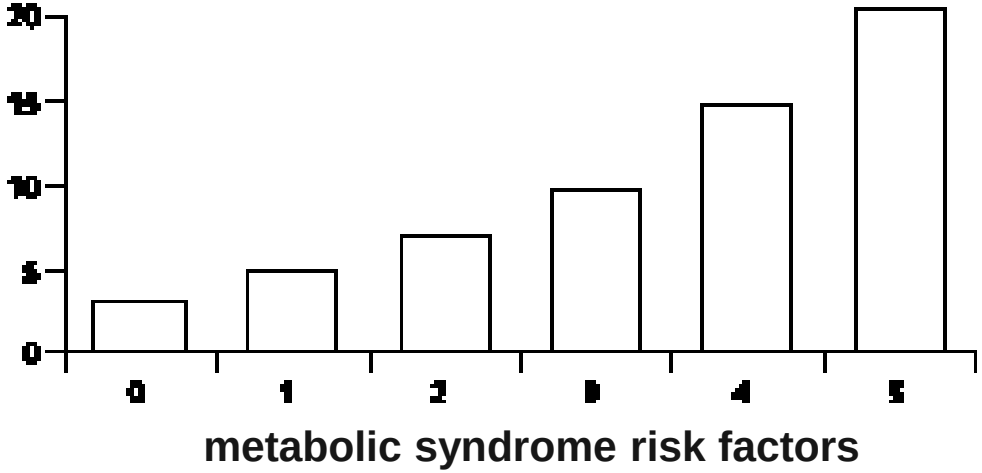
Wang, Kidn.Internat.(2008) 73:19

Metabolic syndrome : risk factor for CKD *(chronic kidney disease)* and microalbuminuria

Prevalence of CKD (%)



Prevalence of microalbuminuria (%)



metabolic syndrome

waist circumference:
>102cm (men)
fasting glucose:
>110mg/dl
HDL-C:
<40mg/dl
triglycerides:
>140mg/dl
blood pressure:
>130/80mmHg

Chen, Ann.Int.Med. (2004) 140:167

Risk *(odds ratio)* of onset of CKD in individuals with 1 or more components of the metabolic syndrome

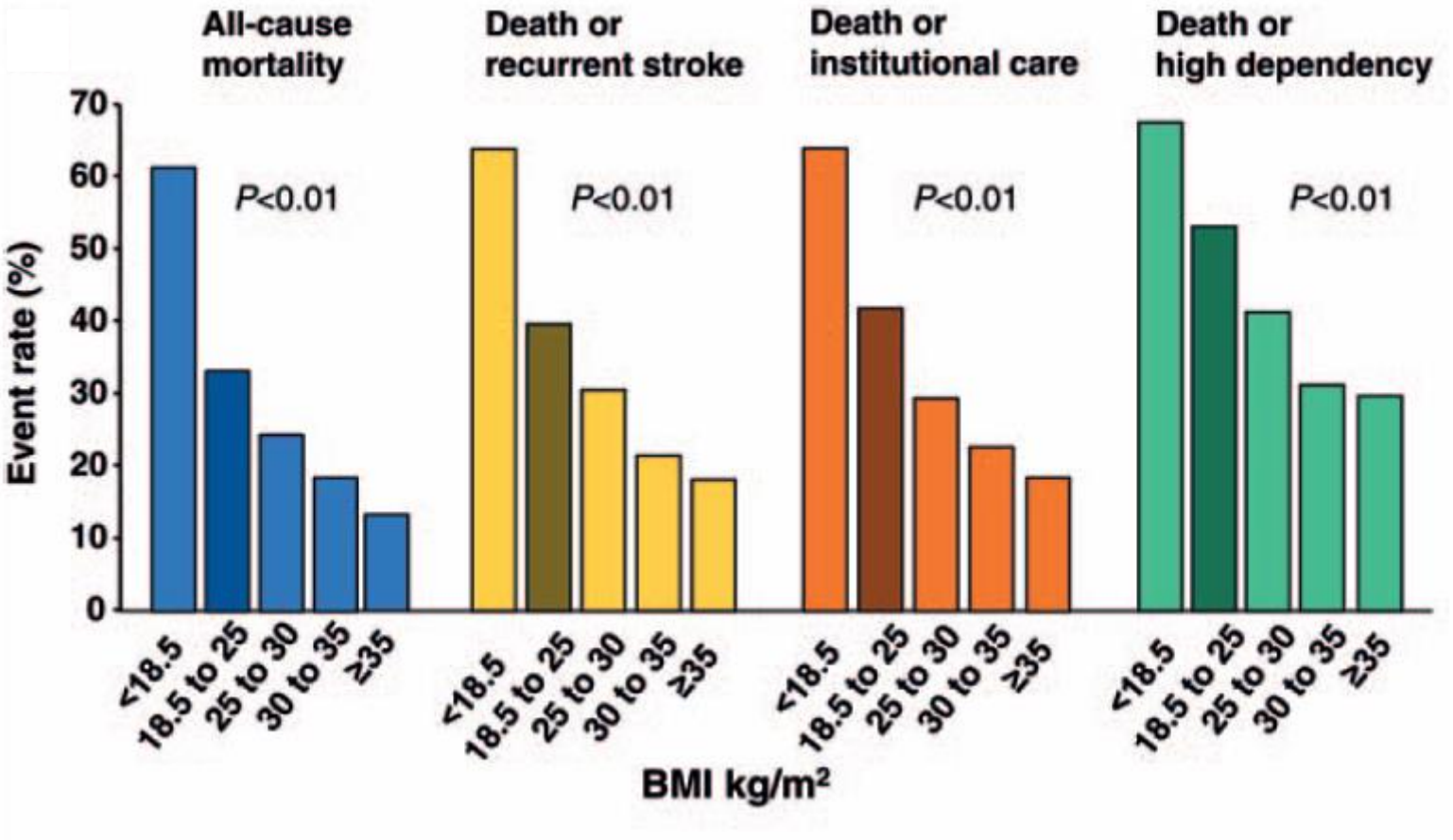
Blood pressure >130/85mm	2.04	<0,001
S-triglycerides >159mg/dl	1.92	„
Plasma-glucose >110mg/dl	1.68	„
S-HDL cholesterol < 40mg/dl	1.63	„
Waist circumference >90cm♂ 80cm♀	1.32	„
Number of components of metabolic syndrome and renal risk		
1 component	1.46	not significant
2 components	1.63	dto
3 components	2.75	dto
4 components	3.56	< 0.001
5 components	4.47	< 0.001

Cheng J.ClinEndocrinol.Metab.(2012) 97:1268

Overweight and Obesity – “Paradox“

with increasing BMI :

better survival. less frequent recurrent stroke and better preservation of function (TEMPIS trial)

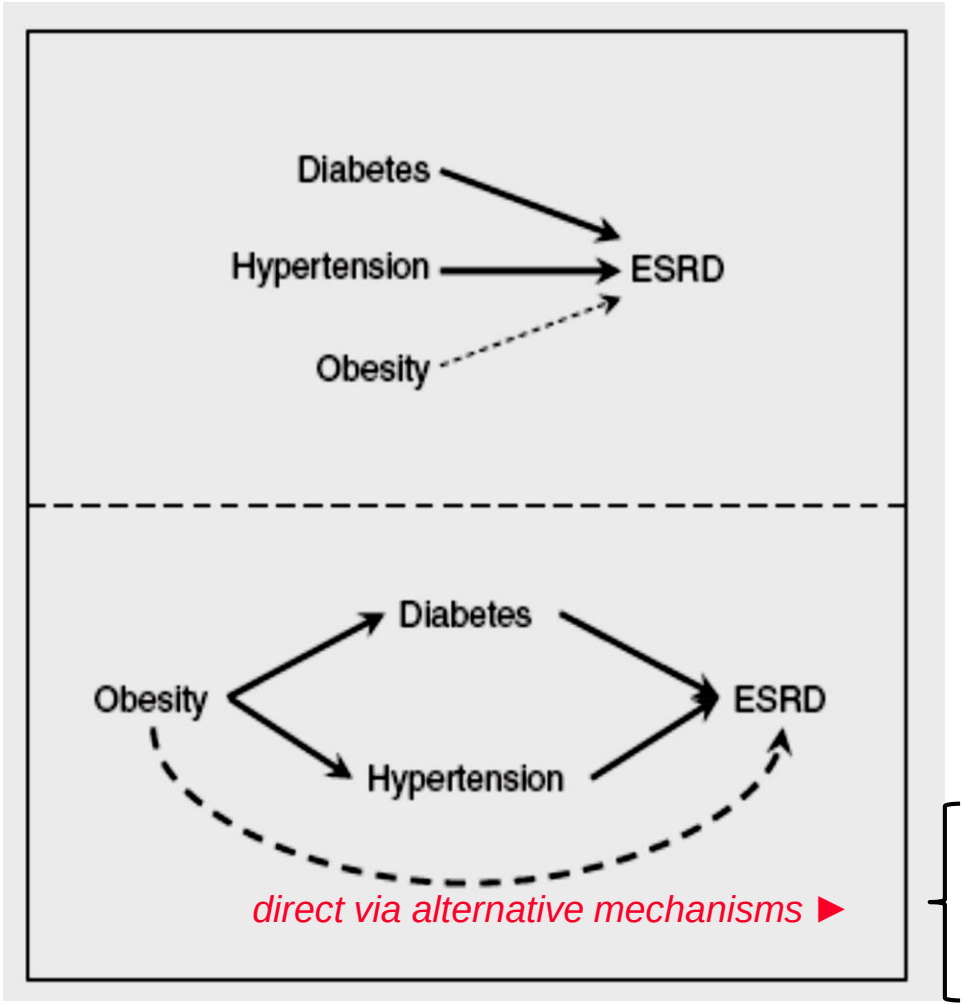


Doehner, Europ Heart J. (2012) 34:268

Link between Obesity and ESRD :

ESRD only the consequence of diabetes and hypertension – or is obesity directly injuring the kidney ?

indirect

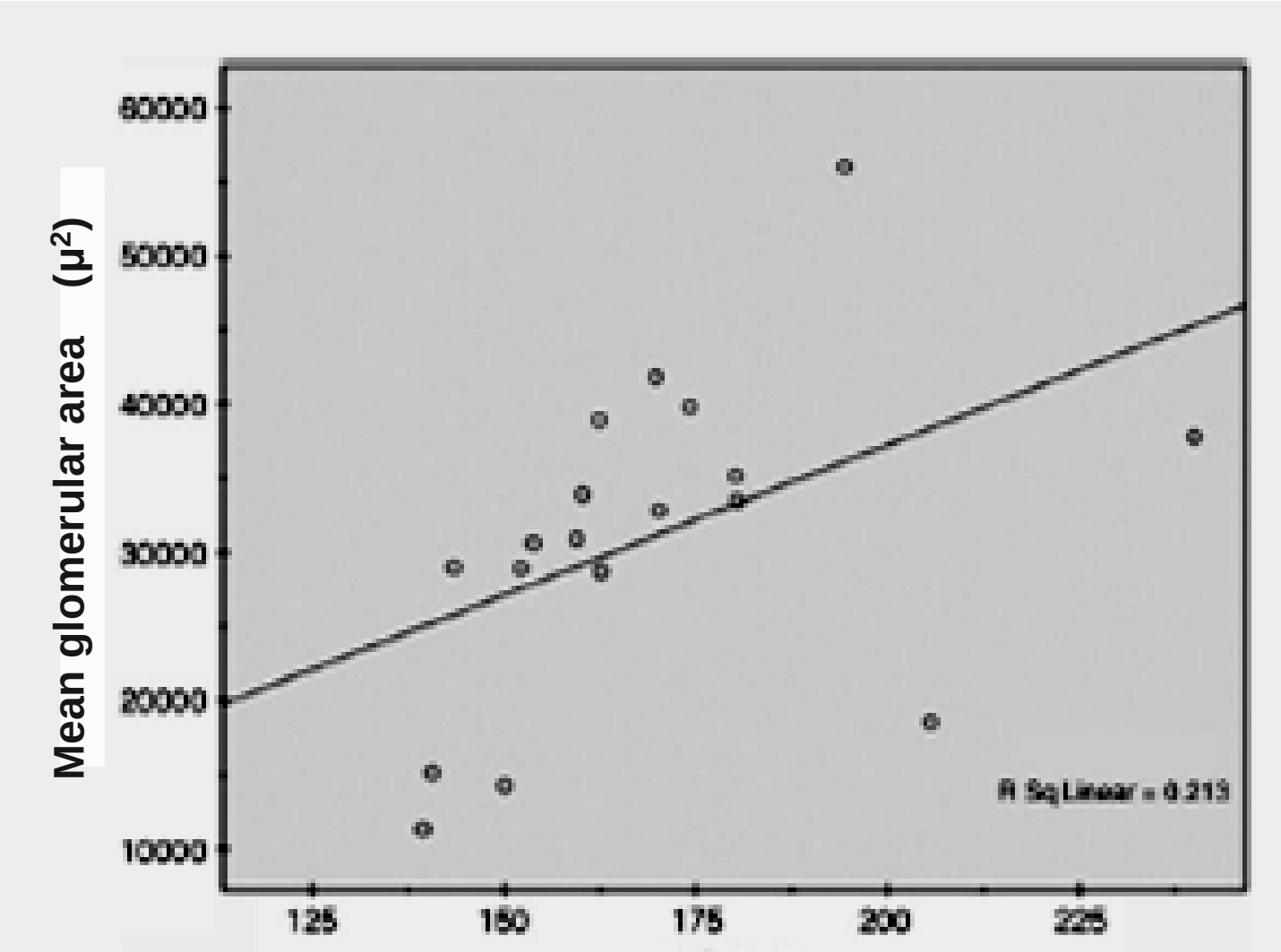


⇨ *direct*

glomerulomegaly
hyperfiltration
glomerulosclerosis
proteinuria
…

Bakker,Nephrol.Dial.Transpl.(2007) 22:15

In extreme obesity
correlation body weight and mean glomerular area



Goumenos, Nephrol.Dial.Transplant.(2009) 24: 3732

High waist-hip-ratio (WHR) impacts on renal hemodynamics

315 healthy persons, BMI 24.9 kg/m^2
GFR ^{125}I-iothalamate109 ml/min/1.73m^2
renal parameters adjusted for BSA

WHR inversely correlated with:

GFR *r= - 0.201; p< 0.001 - lower GFR*

ERPF *r= - 0.431; p<0.001 - lower GFR*

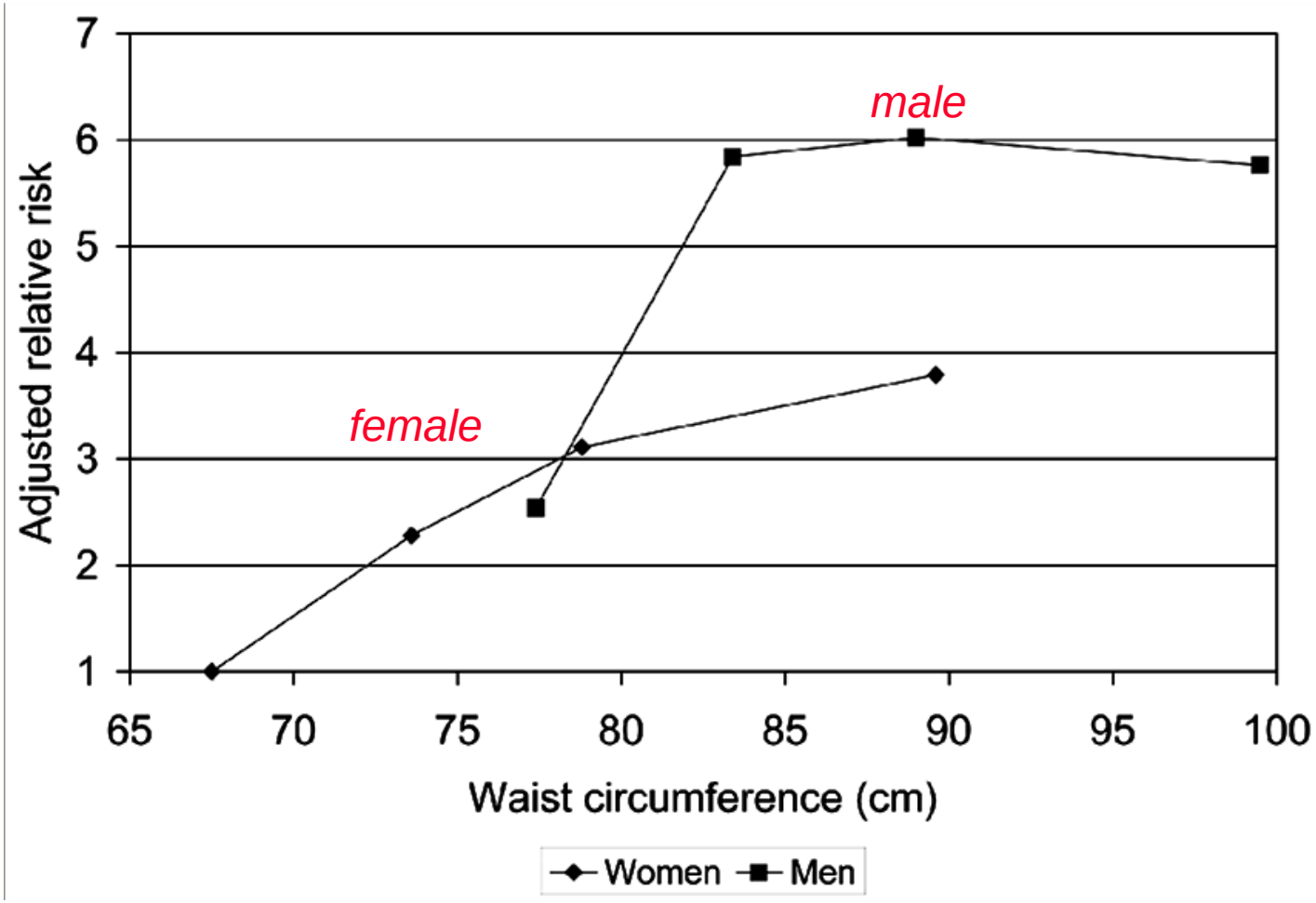
positive correlation with:

FF *r= 0.357; p<0.001 - higher filtration fraction*

Kwakernaak, J.Am.Soc.Nephrol.(2013) 25:987

Central obesity and renal risk: in type 1 diabetes

" waist circumference" predicts onset of microalbuminuria



de Boer, J.Am.Soc.Nephrol.(2007) 18:236