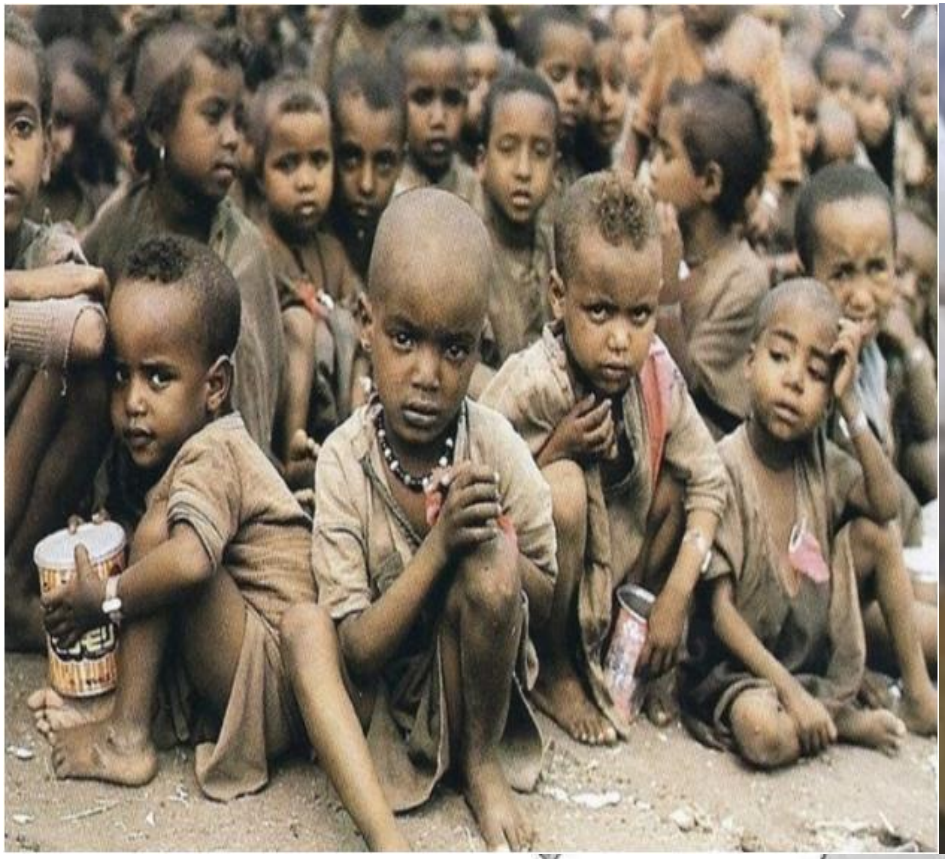
Medical therapy in obesity with focus on CKD

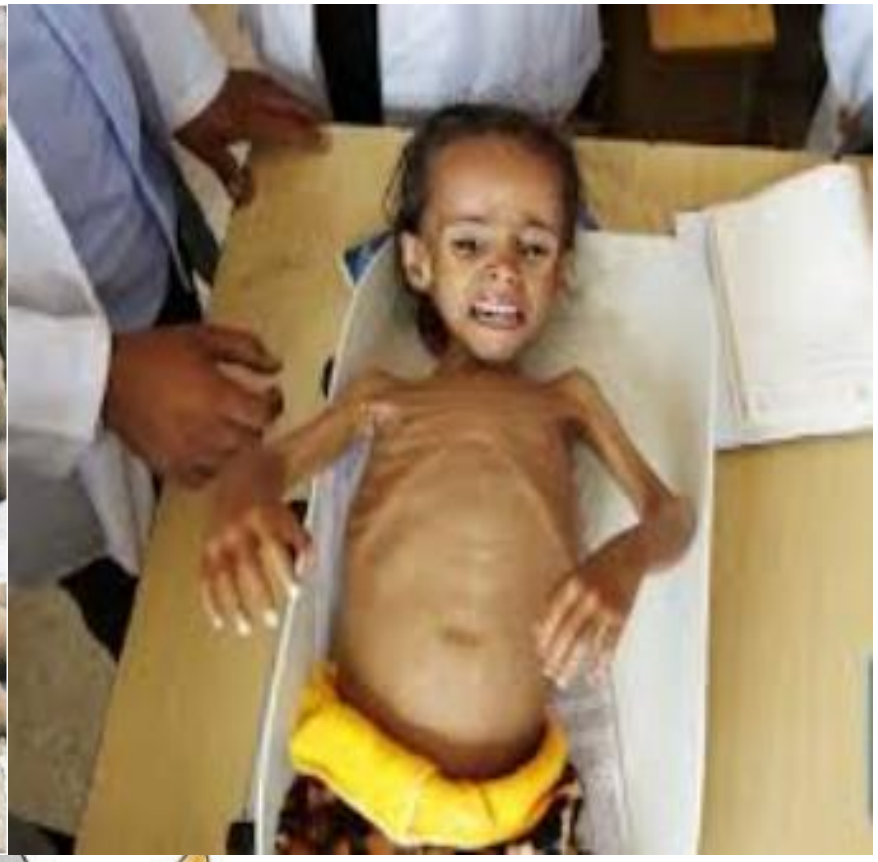
Nahid Hashemi Madani

Institute of Endocrinology and Metabolism

Iran University of Medical Science

How What Was Good Became Ugly and Then Bad





Good

Figure 1. The Venus of Willendorf. Limestone figure from the Late Paleolithic Period, c. 25,000 BC (Naturhistorisches Museum, Vienna, Austria. Reproduced with permission.) Photo credit: Erich Lessing, Art Resource, NY.

Ugly


USA
34%
MEXICO
29.5%
NEW ZEALAND
26.5%
CHILE
25.5%
AUSTRALIA
25%
UNITED KINGDOM
24.5%
CANADA
24%
IRELAND
23%
GREECE
18.5%
SPAIN
17.5%
GERMANY
16%
PORTUGAL
15.5%
ISRAEL
13.5%
FRANCE
11.5%
ITALY
10%
JAPAN
3%

Bad

AACE/ACE 2016

Canadian Task Force 2015

EASO 2015

NICE 2014

JASSO 2016

UAE 2018

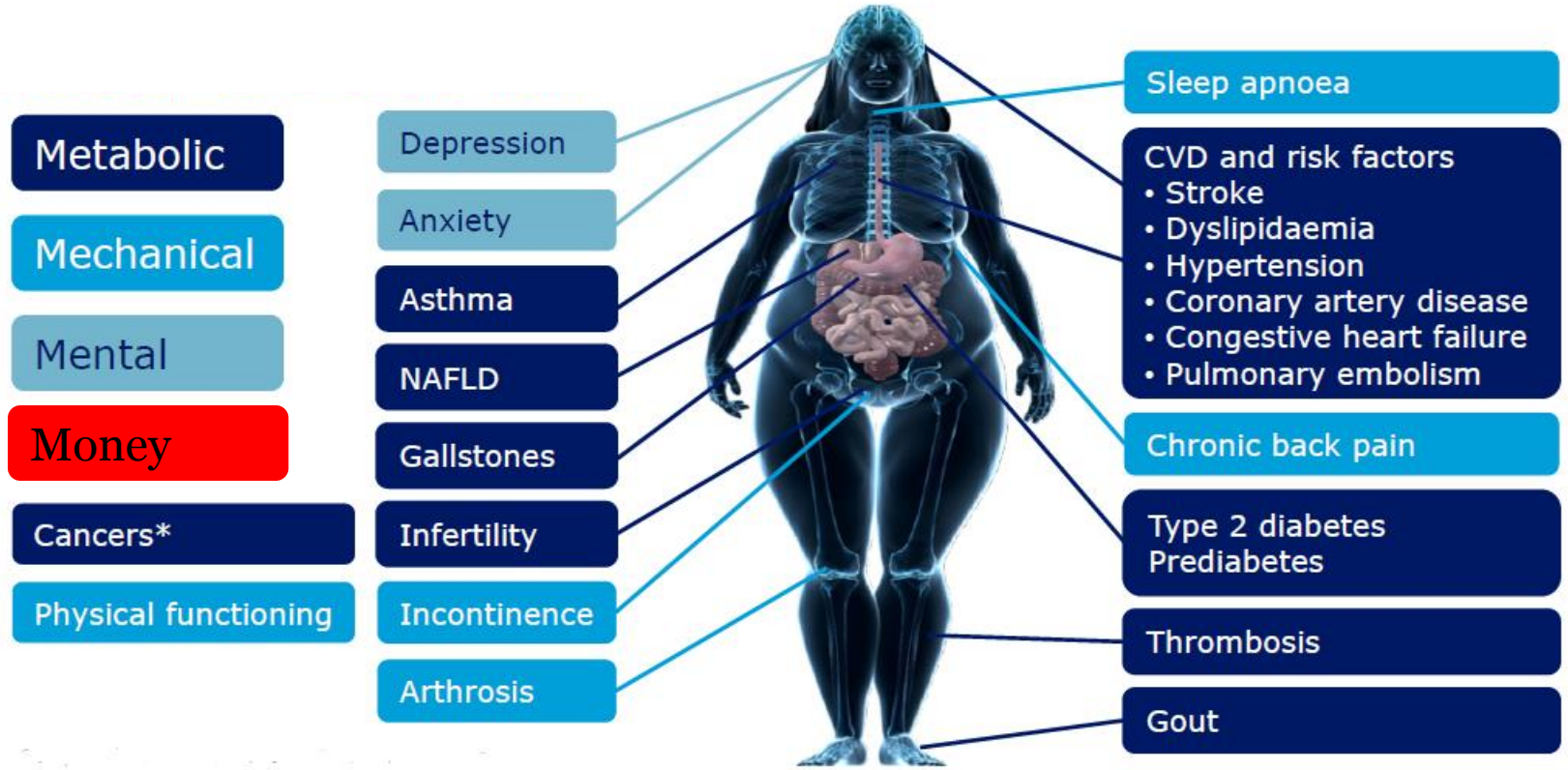
ENDO/ESE/TOS 2015

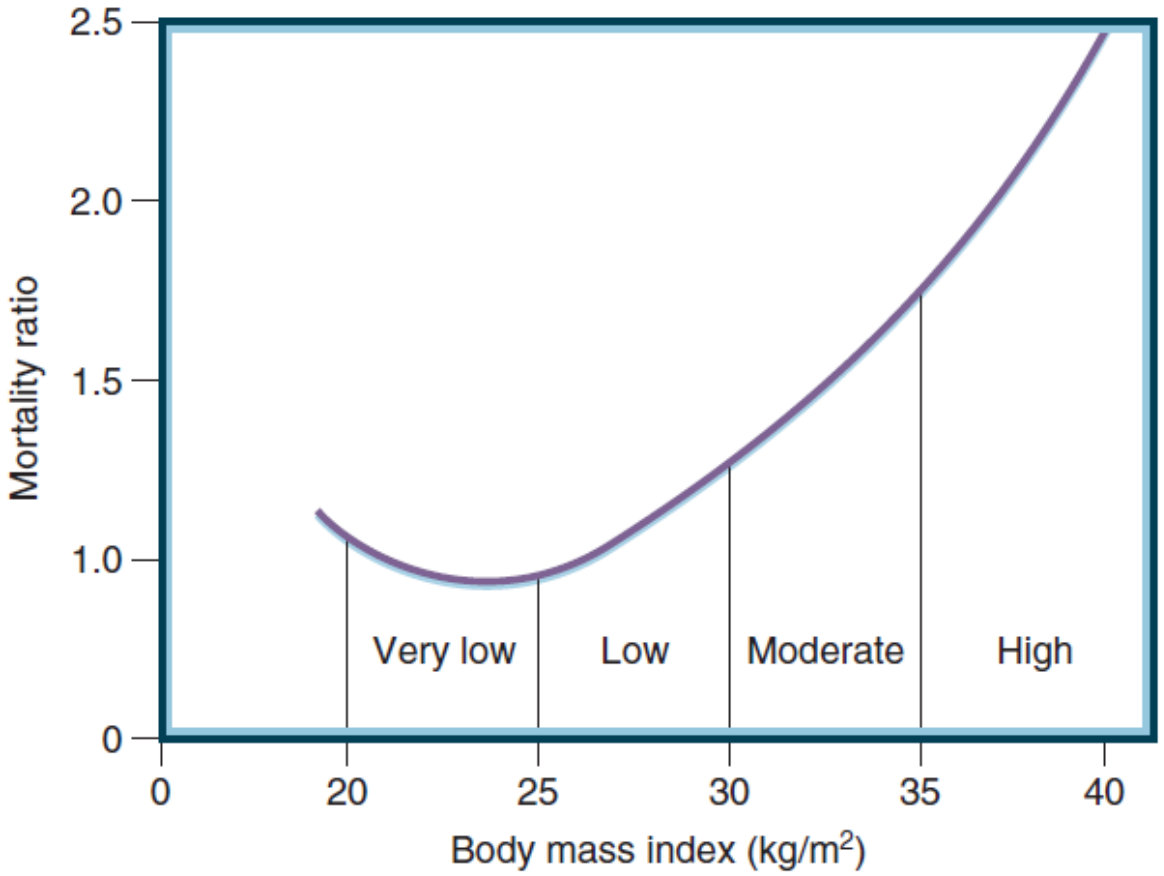
AHA/ACC/TOS 2013

AACE/TOS/ASMBS 2013

IDF 2011

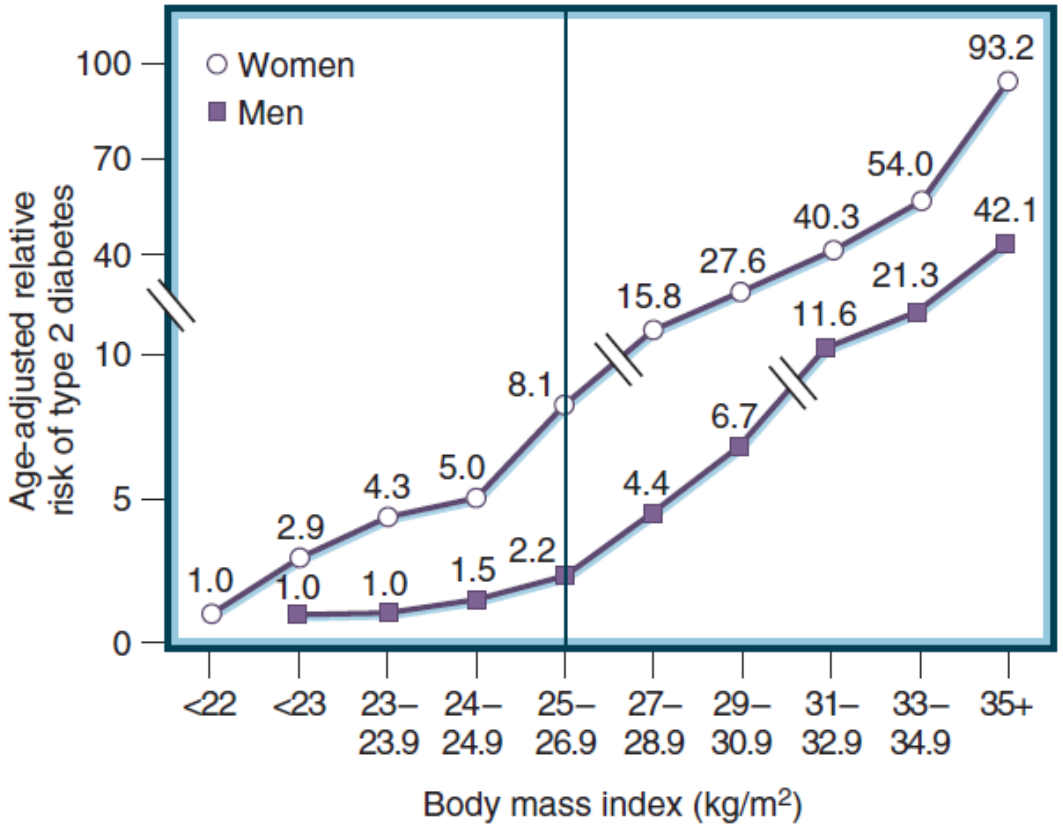
The principal goal in obesity management is to prevent or treat obesity-related comorbidities





Relationship between body mass index and cardiovascular mortality risk in men and women in the United States who never smoked and had no preexisting illness.

Les EA, Garfunkel L. *J Chron Dis.* 1987;32:563



Relationship between body mass index and type 2 diabetes in men and women in the United States.

Colditz GA, Willett WC, Rotnitzky A, et al. *Ann Intern Med.* 1995;122:481-486 .

Defining obesity

WHO guidelines for classifying obesity

WHO classification	BMI cut-off points for definition (kg/m^2)	Cardiovascular disease risk	Asian BMI cut-off points for action (kg/m^2)
Underweight	<18.5		<18.5
Normal range	18.5–24.9	Low	18.5–22.9
Overweight	25.0–29.9	Moderate	≥23.0
Obesity class I	30.0–34.9	High	27.5–32.4
Obesity class II	35.0–39.9	Very high	32.5–37.4
Obesity class III	≥40.0	Very high	≥37.5

World Health Organization. Obesity fact files. (Accessed 30 November 2018)

Defining obesity

Measures used across all guidelines

	Measures used to classify obesity		
	BMI	Waist circumference	Complications
AACE/ACE 2016	✓	✓	
Canadian Task Force 2015	✓		
EASO 2015	✓	✓	✓
NICE 2014	✓	✓	
JASSO 2016	✓		
UAE 2018	✓		
ENDO/ESE/TOS 2015	✓		✓
AHA/ACC/TOS 2013	✓	✓	
EASD/ADA 2018	✓		
ADA 2018*	✓		
AACE/TOS/ASMBS 2013*	✓		
IDF 2011*	✓		

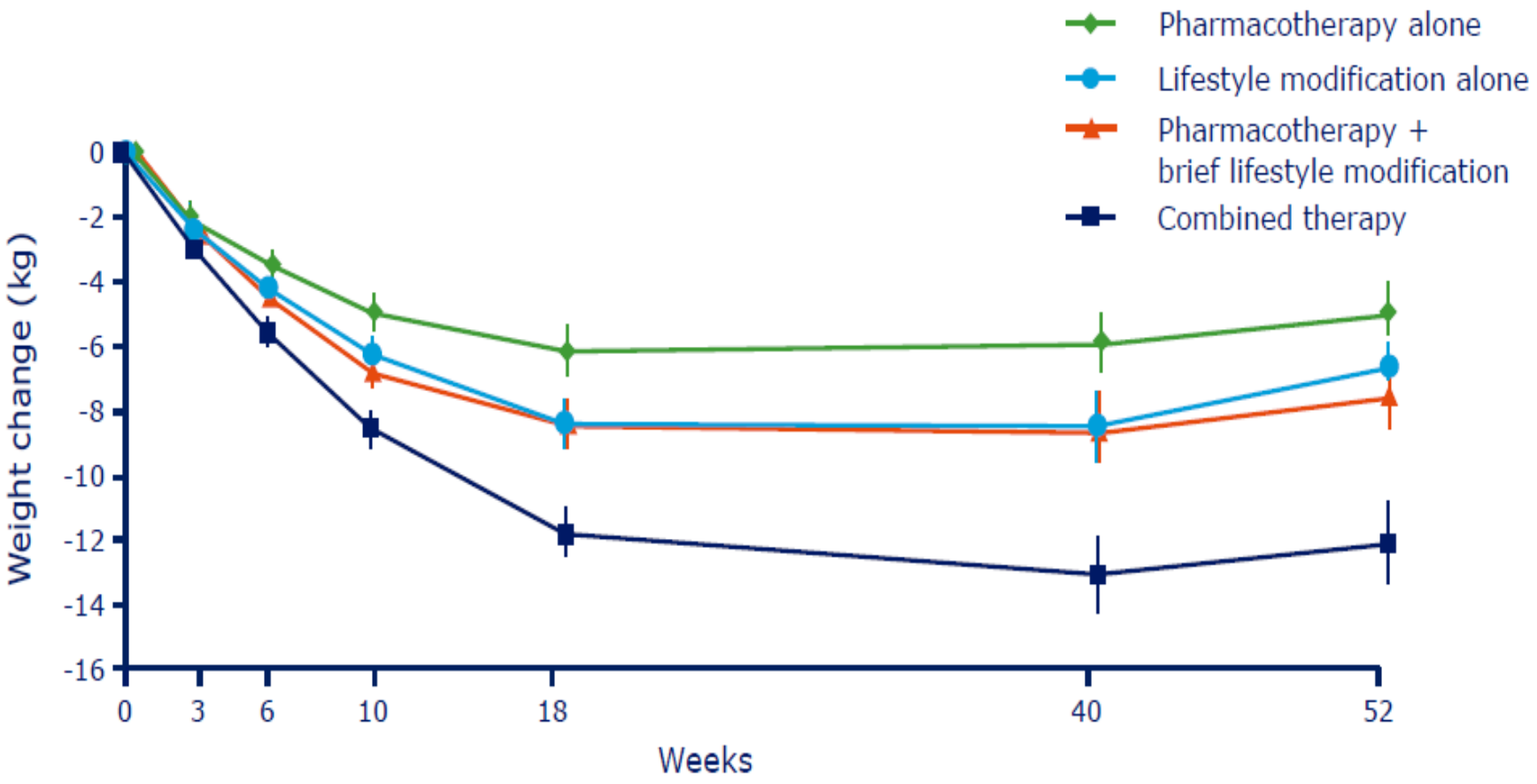
*Only relates to patients with T2D. AACE, American Association of Clinical Endocrinologists; ACC, American College of Cardiology; ACE, American College of Endocrinology; ADA, American Diabetes Association; AHA, American Heart Association; ASMBS, American Society for Metabolic & Bariatric Surgery; EASO, European association for the study of obesity; ENDO, Endocrine Society; ESE, European Society of Endocrinology; IDF, International Diabetes Federation; JASSO, Japan Society for the Study of Obesity; NICE, National Institute for Health and Care Excellence; TOS, The Obesity Society; UAE, United Arab Emirates

EASO: European Guidelines for Obesity Management in Adults 2015

BMI, kg/m²*	WC*, cm		Complications
	Men <94 Women <80	Men ≥94 Women ≥80	
25.0–29.9	Lifestyle intervention	Lifestyle intervention	Lifestyle intervention ± Drugs
30.0–34.9 drug	Lifestyle intervention	Lifestyle intervention ± Drugs	Lifestyle intervention ± Drugs ± Surgery†
35.0–39.9 surgery	Lifestyle intervention ± Drugs	Lifestyle intervention ± Drugs	Lifestyle intervention ± Drugs ± Surgery
≥40.0	Lifestyle intervention ± Drugs ± Surgery	Lifestyle intervention ± Drugs ± Surgery	Lifestyle intervention ± Drugs ± Surgery

Yumuk V, et al. Obes Facts. 2015; 8(6): 402–24

Medical therapy in obesity



Wadden TA, N Engl J Med, 2005, 353: 2111- 2120

- First, **not every drug works for every patient**; individual responses vary widely.
- Second, when the maximal therapeutic effect is achieved, a **plateau** is reached and **weight loss ceases**.
- Finally, **when** drug therapy is **discontinued**, **weight gain** can be expected.

- There are **responders** and **non-responders** to the anti-obesity drugs.

- A **5% weight loss** should be achieved after **3-month** treatment.

- If this is not the case, the **anti-obesity drug should be interrupted.**

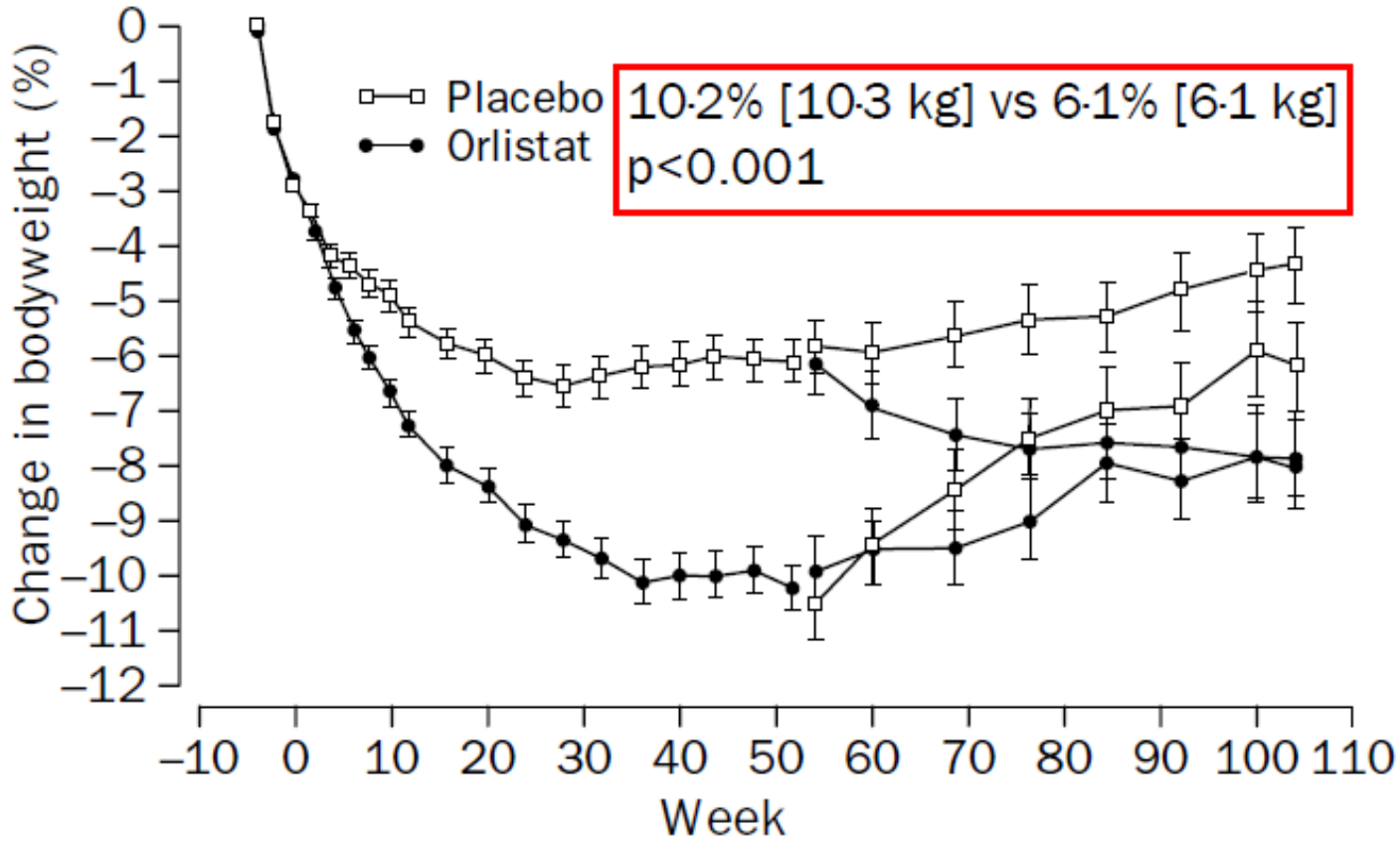
Dominique Durrer Schutz. Obes Facts 2019;12:40–66

Short-term treatment (**3 to 6 months**) using weight-loss medications **has not** been demonstrated to produce **longer-term health benefits** and cannot be generally recommended based on scientific evidence.

AACE/ACE Obesity CPG, *Endocr Pract.* 2016;22

			**Mode of action**
Orlistat (Xenical, Alli)	√	√	Energy wastage
Phentermine/topiramate (Qsymia)	×	√	Appetite suppression
Lorcaserin (Belviq, Belviq XR)	×	√	Appetite suppression
Naltrexone/bupropion (Mysimba, Contrave)	√	√	Appetite suppression
Liraglutide 3.0 mg (Saxenda)	√	√	Appetite suppression

Antiobesity medication **Year of FDA approval**	**Mechanism of action**	**Dose**	**Common side effects**	**Contraindication**	**Monitoring and comments**
Orlistat 1999	Lipase inhibitor	60-120 mg Before meal	Steatorrhea Fecal urgency Incontinance Decreased absorption of fat soluble vitamines Warfarin (enhance) Anti-epileptics (decrease) Levothyroxine (decrease) **Cyclosporine (decrease)**	Pregnancy Breaast feeding Chronic malabsorption Cholestasis	Cholelitiasis **Nephrolitiasis** Recommend standard multivitamin (to include vitamins A,D, E, and K) at bedtime or 2 hours after orlistat dose



Lars Sjöström, et al, THE LANCET, 1998, Vol 352.

- Trials have found that **Orlistat**, when used in combination with a diet and lifestyle program, leads to a **modest reduction in weight in CKD patients .**

- There are concerns that Orlistat can increase the risk of **oxalate nephropathy** and **renal stones** particularly in patients with renal impairment .

- **No studies** currently exist evaluating the **safety or efficacy** in **renal transplant populations.**

- As Orlistat interferes with cyclosporine absorption , and it should not be prescribed to patients on Cyclosporin.

- The effect of Orlistat on calcineurin inhibitors such as Tacrolimus have also not been tested.

Lambert, Kelly, et al 2018, DOI: 10.1111/nep.13118

Anti obesity medication Year of FDA approval	Mechanism of action	Dose	Common side effects	Contraindication	Monitoring and comments
Lorcaserin 2012	Serotonin (5HT2c) receptor agonist (reduces appetite and food intake)	10 mg BID 3.6% 1 year	Headache Nausea Dry mouth Dizziness Fatigue constipation	Pregnancy Breast feeding Concomitant use of SSRI, SNRI, MAOI	Symptoms of cardiac valve disease Bradycardia Serotonin syndrome Neuroleptic malignant syndrome Depression

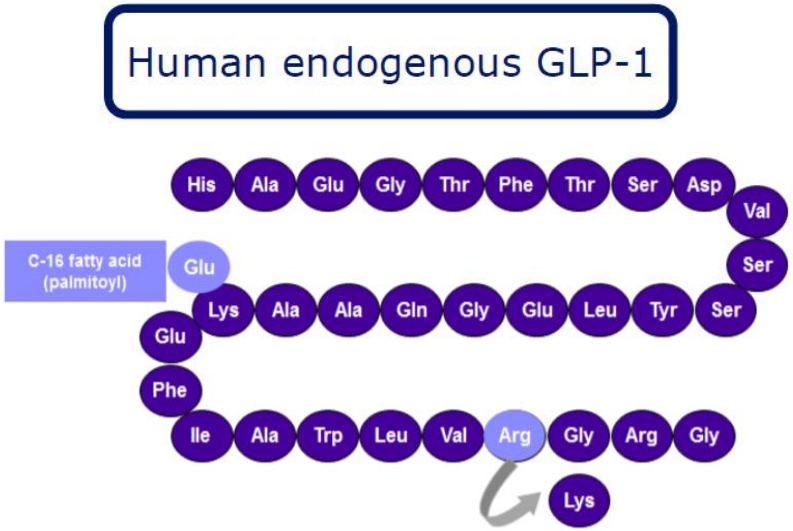
Anti obesity medication Year of FDA approval	Mechanism of action	Dose	Common side effects	Contraindication	Monitoring and comments
Phentermine/ Topiramate 2012	NE release (P) GABA modulation (T) (suppresses appetite)	starting dose: 3.75/23 qd recommended dose: 7.5/46 qd high dose: 15/92 qd 1yr: 6.6% (recommended dose) 8.6% (high dose)	insomnia dry mouth constipation Paresthesia dizziness dysgeusia	Pregnancy breast feeding glaucoma hyperthyroidism Concomitant MAOI use (within 14 days)	Increased heart rate **Hypokalemia (especially with HCTZ or furosemide)** **Acute kidney stone formation** Hypoglycemia in patients having T2DM treated with insulin and/or sulfonylureas

Anti obesity medication Year of FDA approval	Mechanism of action	Dose	Common side effects	Contraindication	Monitoring and comments
Bupropione/ naltrexone 2014	DA/NE reuptake inhibitor(B) opioid antagonist (N)	8/90 mg tb 2 tb bid (titrate during 4 wk) 4.8% 1 year	Nausea constipation Headache vomiting dizziness	uncontrolled hypertension seizure anorexia nervosa / bulimia drug or alcohol withdrawal	Increased HR and BP Worsening of migraines Liver injury (naltrexone) Hypoglycemia in patients T2DM Seizures (bupropion)

Anti obesity medication Year of FDA approval	Mechanism of action	Dose	Common side effects	Contraindication	Monitoring and comments
Liraglutide (saxenda) 2014	GLP-1 agonist	3 mg/day/sc	nausea, vomiting, pancreatitis	medullary thyroid cancer history MEN type 2 history	acute pancreatitis acute gall bladder disease Increased heart rate Injection site reactions

What is GLP-1?

- GLP-1 is a peptide comprised of 31 amino acids
- Member of incretin family
- Secreted predominantly from L-cells in the gut, but also the brain (nucleus tractus solitarius)

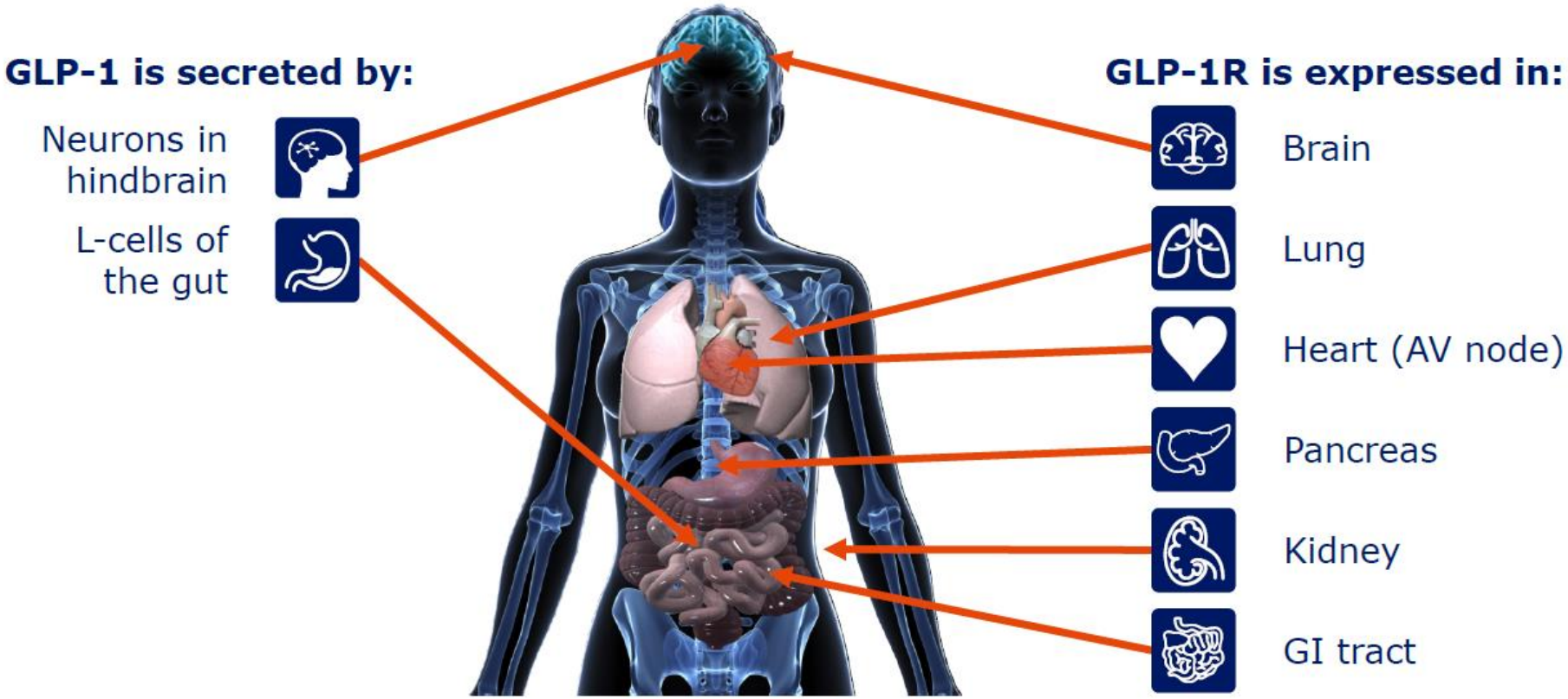


Enzymatic degradation by DPP-4

$t_{½}$=1.5–2 min

Merchenthaler *et al. J Comp Neurol* 1999;403:261–80; Baggio, Drucker. *Gastroenterology* 2007;132:2131–57; Ducker, Nauck. *Lancet* 2006;368:1696–705

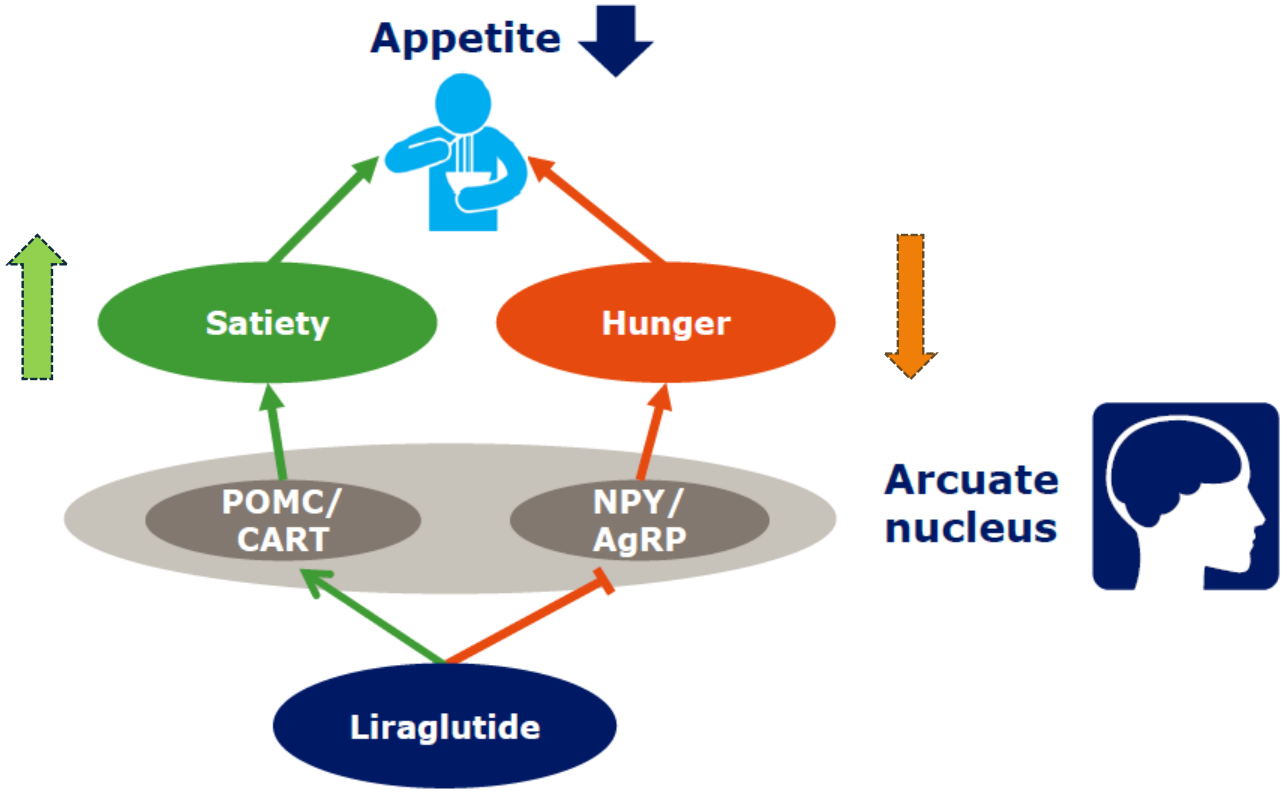
GLP-1 secretion and receptor expression



Merchenthaler *et al. J Comp Neurol* 1999;403:261–80; Baggio, Drucker. *Gastroenterology* 2007;132:2131–57;
Ban *et al. Circulation* 2008;117:2340–50**;** Vrang *et al. Prog Neurobiol* 2010;92:442–62; Pyke *et al. Endocrinology* 2014;155:1280–90

Liraglutide increases satiety and reduces hunger

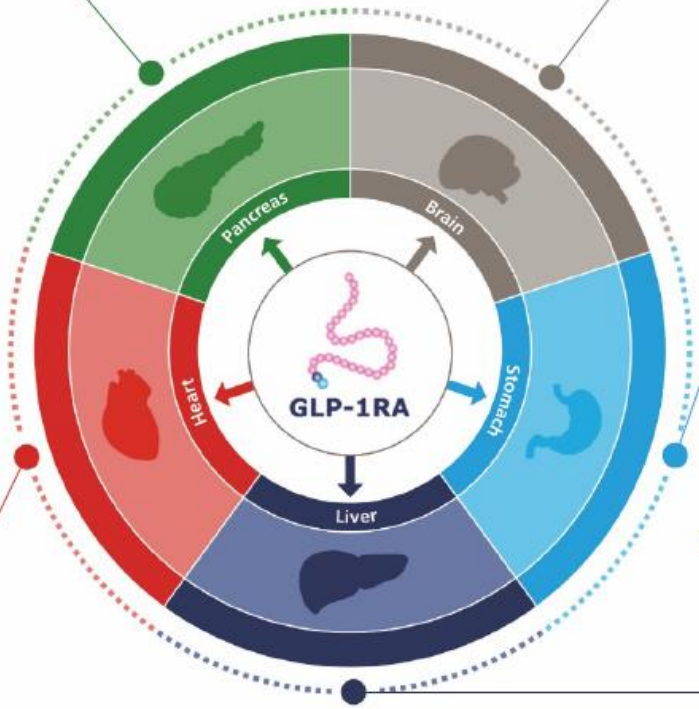
Via neurons in the arcuate nucleus



Secher *et al. J Clin Invest* 2014;124:4473–88; van Can *et al. Int J Obes (Lond)* 2014;38:784–93

GLP-1RAs have multifactorial effects

Pharmacological effects of GLP-1RAs



Pancreas

- ↑ Beta-cell function[1]
- ↓ Beta-cell apoptosis[1]
- ↑ Insulin biosynthesis[1]
- ↑ Glucose-dependent insulin secretion[1]
- ↓ Glucose-dependent glucagon secretion[1]

Brain

- ↓ Body weight[5]
- ↓ Food intake[6]
- ↑ Satiety[7,8]

Stomach

- ↓ Gastric emptying[9]

Liver

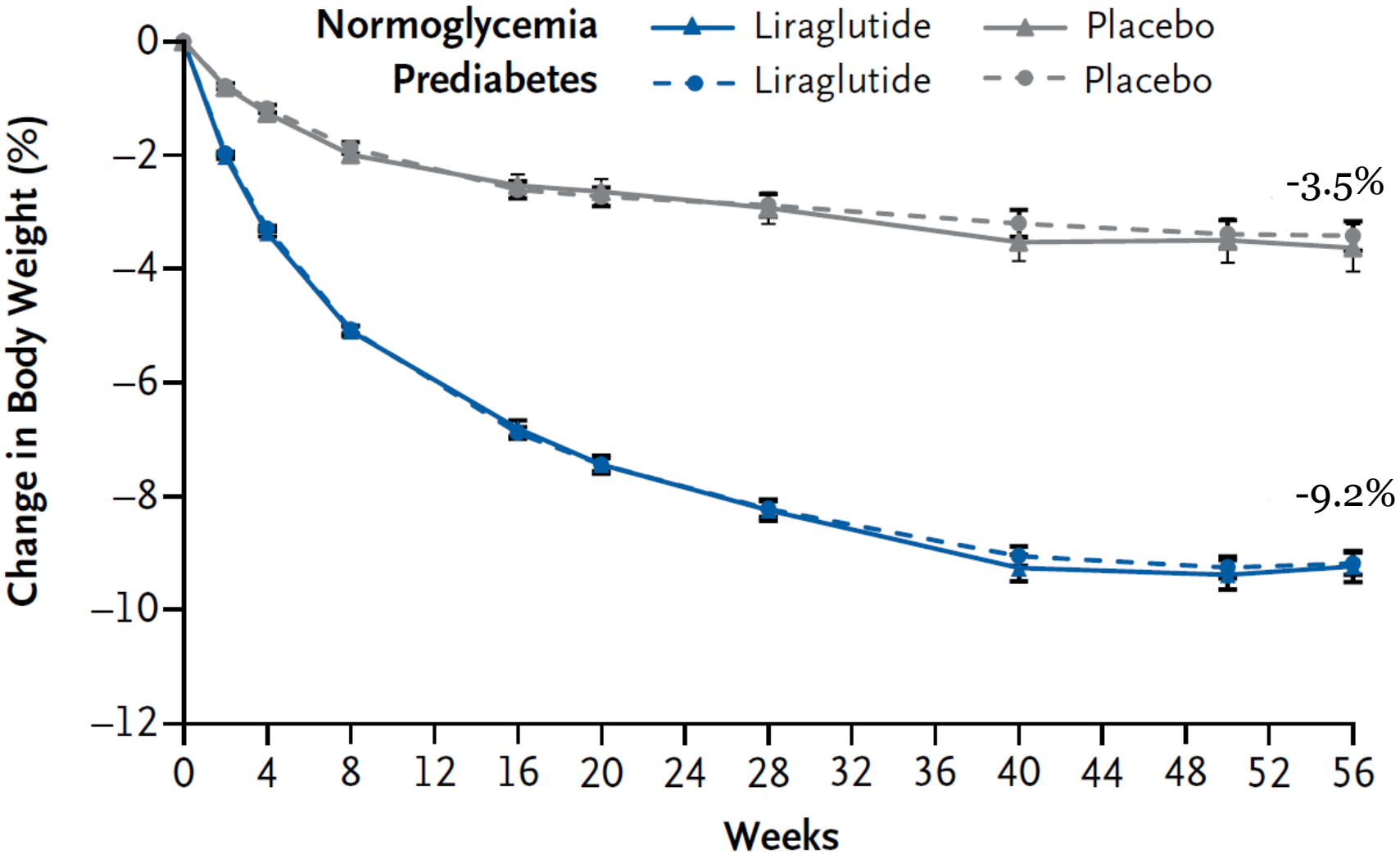
- ↓ Endogenous glucose production[10]
- ↑ Hepatic insulin sensitivity[10]
- ↓ *De novo* lipogenesis[10]
- ↓ Lipotoxicity[10]
- ↓ Steatosis[11]

Heart

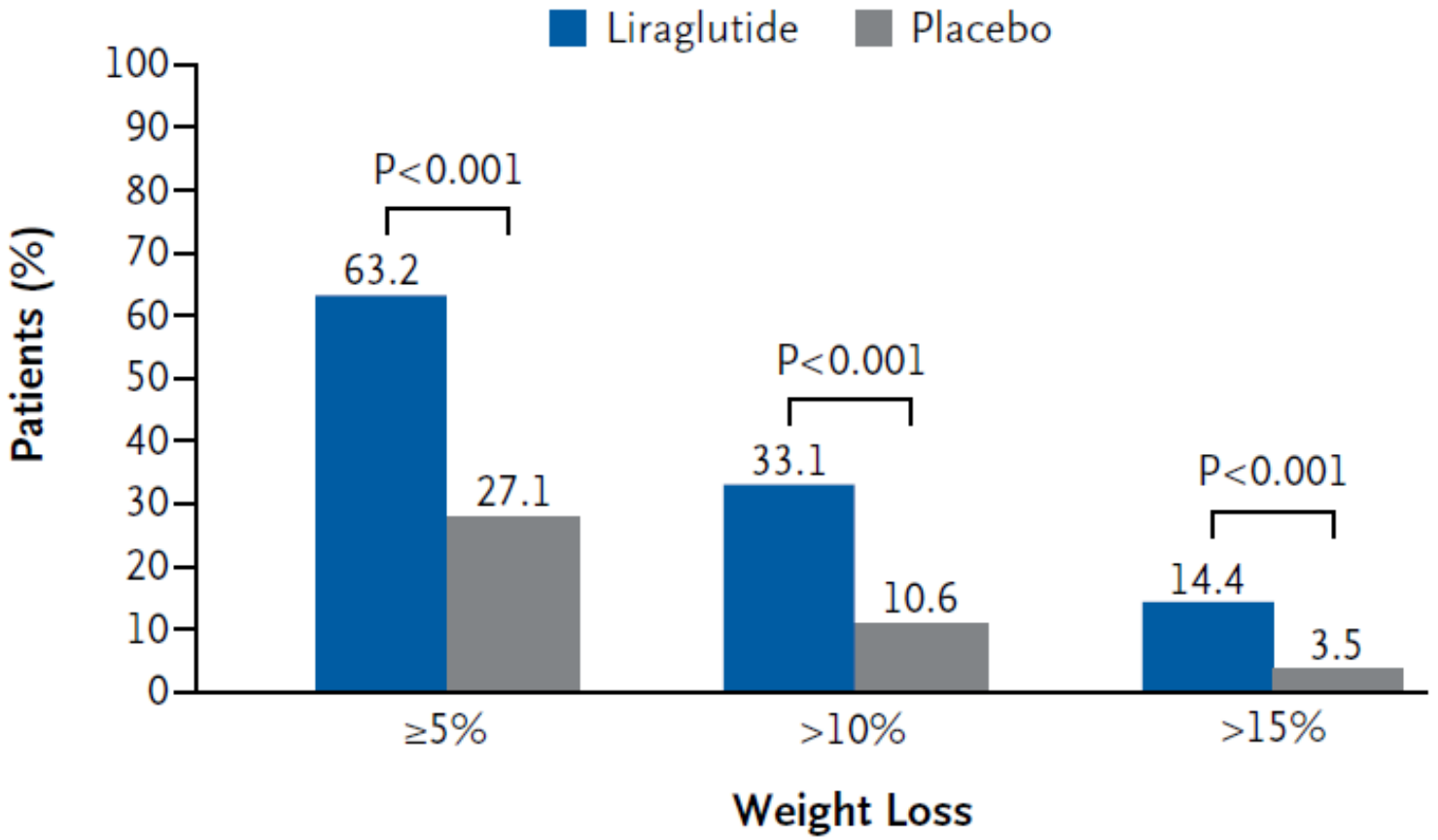
- ↓ Cardiovascular risk[2]
- ↓ Fatty acid metabolism[3]
- ↑ Cardiac function[3]
- ↓ Systolic blood pressure[3]
- ↓ Inflammation[4]

Adapted from Campbell & Drucker. *Cell Metab* 2013;17:819–37; Pratley & Gilbert. *Rev Diabet* Stud 2008;5:73–94.

N:3731



Pi-Sunyer *et al. N Engl J Med* 2015;373:11–22



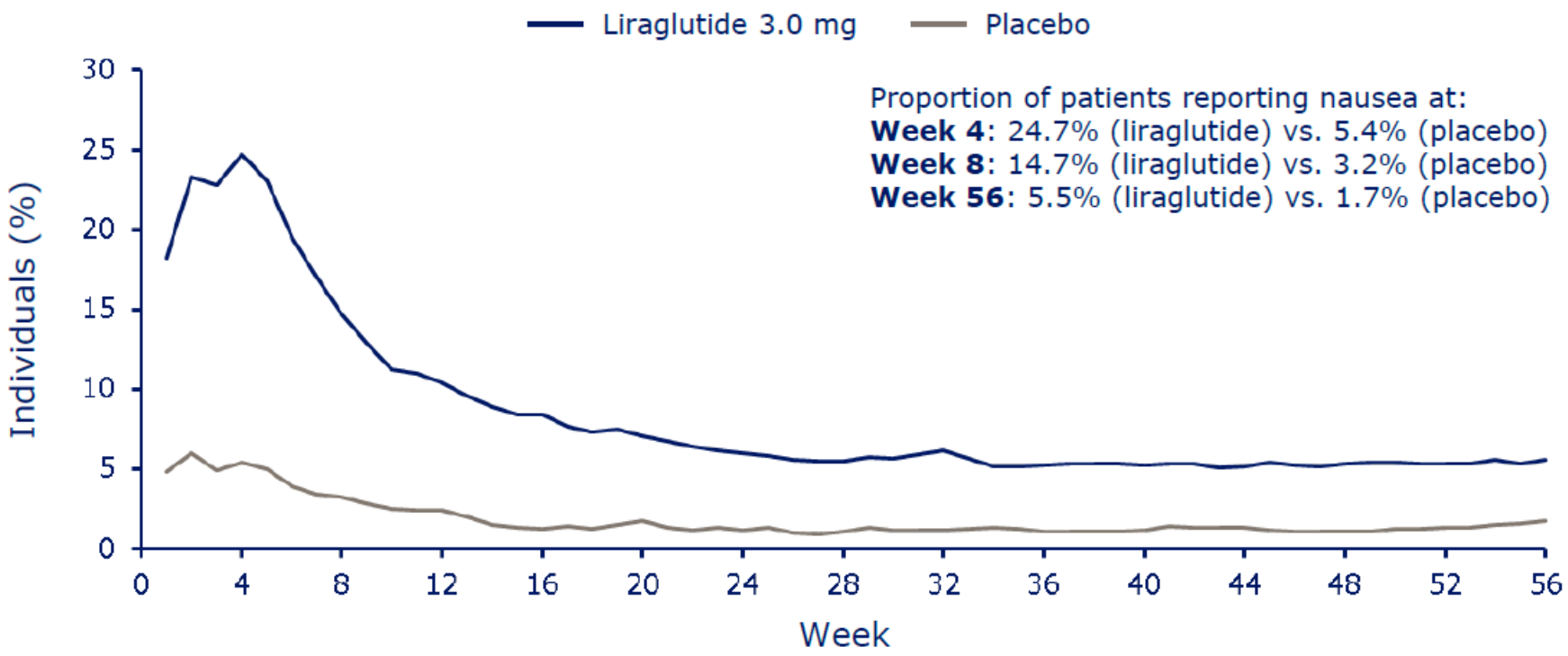
Pi-Sunyer *et al. N Engl J Med* 2015;373:11–22

Changes in Cardiometabolic Risk Factors between Baseline and Week 56

End Point	Liraglutide (N = 2437)	Placebo (N = 1225)	Estimated Treatment Difference, Liraglutide vs. Placebo (95% CI)†	P Value
Vital signs				
Systolic blood pressure (mm Hg)	−4.2±12.2	−1.5±12.4	−2.8 (−3.56 to −2.09)	<0.001
Diastolic blood pressure (mm Hg)	−2.6±8.7	−1.9±8.7	−0.9 (−1.41 to −0.37)	<0.001
Pulse (beats/min)	2.5±9.8	0.1±9.5	2.4 (1.9 to 3.0)	<0.001
Fasting lipid profile				
Cholesterol (%)				
Total	−3.1	−1.0	−2.3 (−3.3 to −1.3)	<0.001
LDL	−3.0	−1.0	−2.4 (−4.0 to −0.9)	0.002
HDL	2.3	0.7	1.9 (0.7 to 3.0)	0.001
VLDL	−13.1	−5.5	−9.1 (−11.4 to −6.8)	<0.001
Non-HDL	−5.1	−1.8	−3.9 (−5.2 to −2.5)	<0.001
Triglycerides	−13.3	−5.5	−9.3 (−11.5 to −7.0)	<0.001
Free fatty acids	1.7	3.5	−4.2 (−7.3 to −0.9)	0.01

Proportion of individuals with nausea

0–56 weeks



Pi-Sunyer *et al. N Engl J Med* 2015;373:11–22

- There have been reports of **acute renal failure with saxenda**, sometimes requiring hemodialysis.

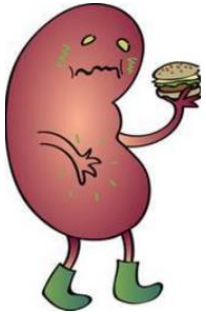
- A majority of the reported events occurred in patients who had experienced **nausea, vomiting, or diarrhea leading to volume depletion**.

- There is **limited experience** with Saxenda in patients with **mild, moderate, and severe renal impairment**, including end-stage renal disease.

- Saxenda should be used with **caution** in this patient population.

- Saxenda shoud be avoided in **GFR<30**

SAXENDA – FDA https://www.accessdata.fda.gov › drugsatfda_docs



Identification of Adults with CKD Who Will Benefit from Weight Loss

- Decrease the rate of CKD progression
- Decrease albuminuria
- Improve HTN, DM,DLP, CVD outcomes
- Decrease mortality

Obesity paradox

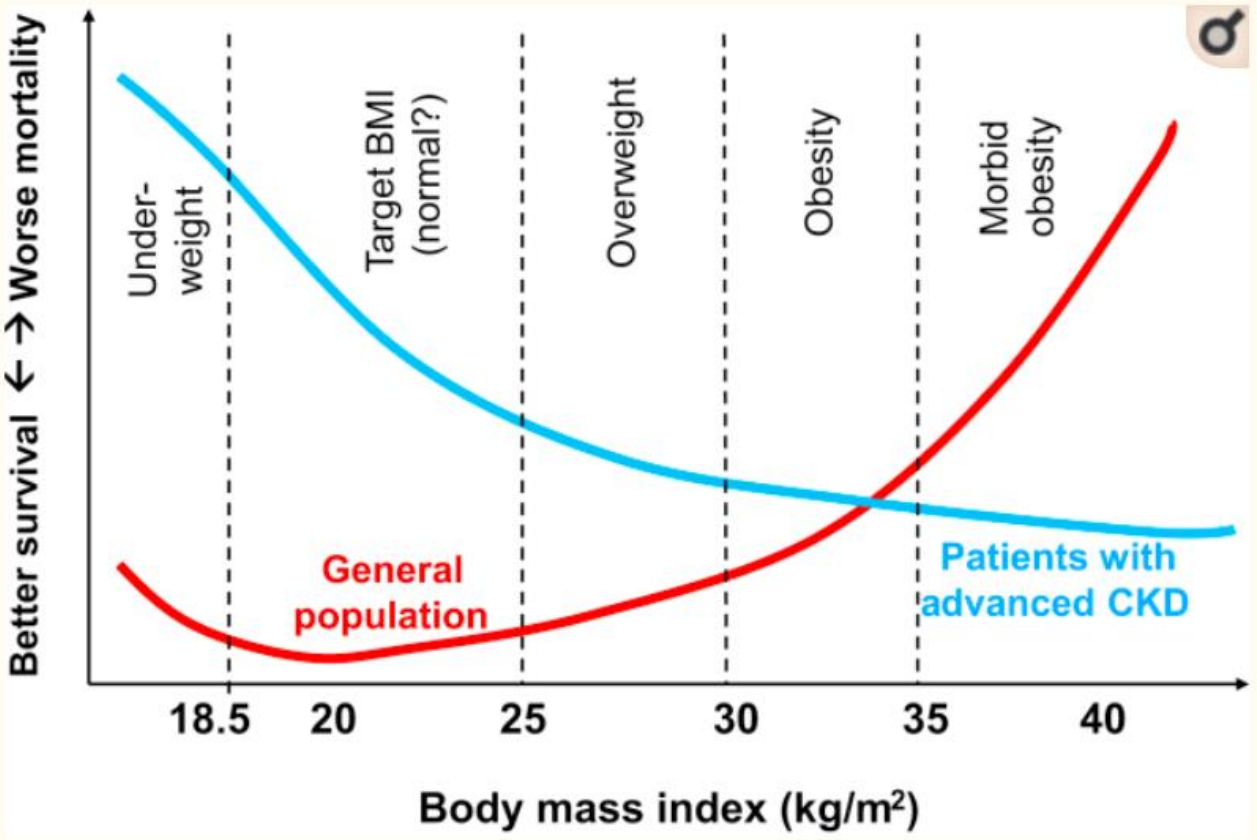


Figure 1

Reverse association of body mass index (BMI) and survival in patients with advanced chronic kidney disease (CKD) as compared to the general population.

Kamyar Kalantar- Zadeh, Kidney Int Rep (2017) 2, 271–281

- Non-dialysis dependent – chronic kidney disease
- Hemodialysis patients
- peritoneal dialysis patients
- Candidate for kidney transplant
- kidney transplant recipients

Non-dialysis dependent–chronic kidney disease

Table 2. Changes in Clinical and Biochemical Variables in the Two Groups

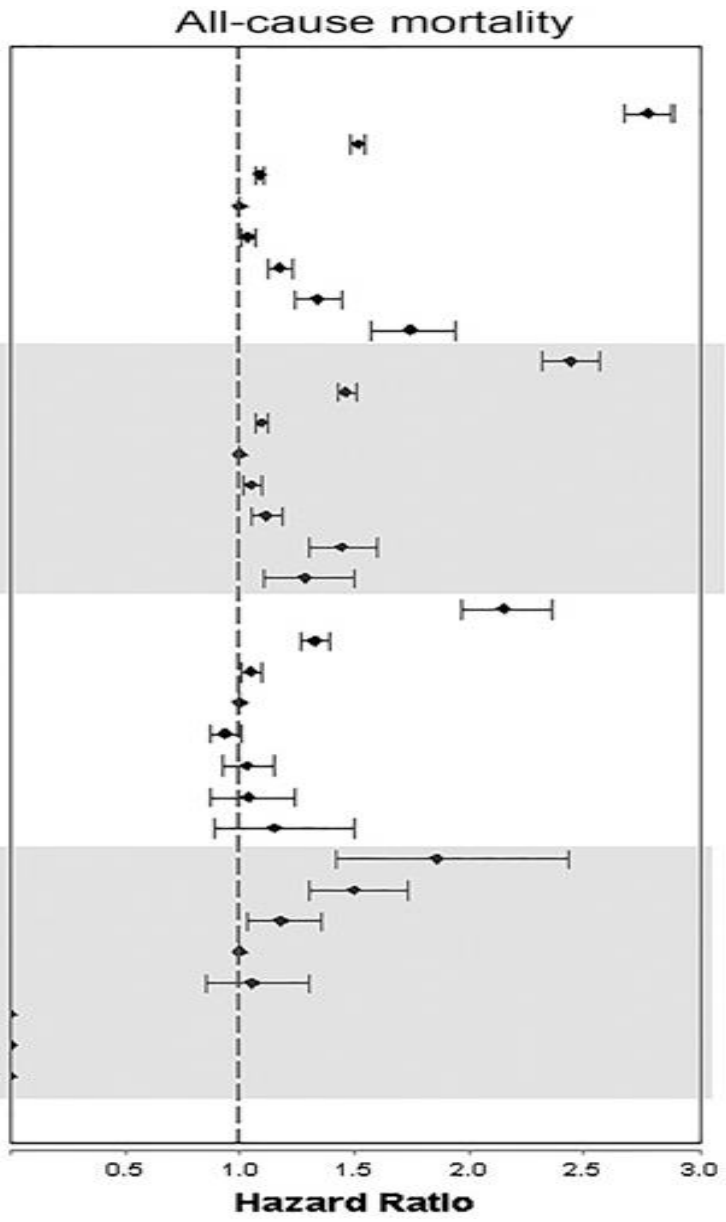
N: 30 CKD; Stage1-2

	Diet Group			Control Group		
	Baseline	Month 1	Month 5	Baseline	Month 1	Month 5
Weight (kg)	87.5 ± 11.1 (62.2-103.6)	85.5 ± 10.7*† (61.5-101.7)	83.9 ± 10.9*†‡ (57.7-102.8)	96.1 ± 16.6 (77.4-133.5)	96.5 ± 16.3 (79.6-134)	98 ± 16.4*†§ (81.1-135.2)
BMI (kg/m^2)	33 ± 3.5 (28-42.2)	32.2 ± 3.2*† (27.2-40.2)	31.6 ± 3.2*†‡ (26.7-40)	34.3 ± 5.7 (27.9-47.8)	34.5 ± 5.7 (27.8-48)	35 ± 5.8*†§ (27.7-48.4)
Systolic blood pressure (mm Hg)	140 ± 24.1 (110-210)	141.8 ± 20.5 (110-180)	138.5 ± 14.1 (110-160)	135 ± 12.4 (120-160)	140.4 ± 8 (130-155)	140.4 ± 18.3 (110-170)
Diastolic blood pressure (mm Hg)	79.6 ± 8.3 (70-90)	80.4 ± 9.3 (65-95)	76.6 ± 8.8 (69-96)	83 ± 9.7 (70-100)	84.3 ± 9.2 (69-98)	88.5 ± 11.1 (60-100)
Serum creatinine (mg/dL)	1.5 ± 0.7 (0.7-3.2)	1.4 ± 0.8 (0.6-3.4)	1.5 ± 0.8 (0.7-3.5)	1.6 ± 0.5 (1-2.7)	1.8 ± 0.6 (1-3)	1.8 ± 0.6*† (1.2-2.9)
Creatinine clearance (mL/min/1.73 m^2)	68.1 ± 33.6 (25.9-151.2)	69.2 ± 33.8 (24.2-131.2)	67 ± 34.1 (26.4-129.8)	61.8 ± 22.1 (29.8-90.7)	56.92 ± 21.7* (26.5-90.3)	56 ± 19.9*† (27.7-83.5)
Total cholesterol (mg/dL)	213.2 ± 52.5 (115-330)	216.9 ± 52.6 (128-318)	210.8 ± 38.8 (134-298)	209.3 ± 39.5 (148-263)	222.1 ± 36.4 (159-269)	224.6 ± 36.4* (160-265)
HDL cholesterol (mg/dL)	41.4 ± 11.9 (21-67)	45.2 ± 8.8 (33-63)	53.6 ± 10.2*†§ (38-67)	41.5 ± 10.6 (26-59)	46.3 ± 11.7 (34-64)	59.6 ± 31.1* (34-138)
LDL cholesterol (mg/dL)	142.2 ± 35.2 (62-190)	149.4 ± 44.6 (60-241)	131.5 ± 27.6§ (73-172)	133.5 ± 32.1 (84-175)	141.3 ± 25.5 (102-185)	128.9 ± 36.2 (84-193)
Triglycerides (mg/dL)	114 ± 50.6 (48-250)	110.5 ± 31.4 (58-160)	112.4 ± 41.7 (58-222)	141.8 ± 41.5 (91-229)	151.9 ± 55.6 (84-264)	179.2 ± 81.4 (71-298)
Urinary sodium (mEq/24 h)	209.8 ± 58.5 (124-324)	194.7 ± 58.6 (100-320)	201.2 ± 57 (95-339)	192 ± 95.5 (54-364)	166.4 ± 61.4 (69-241)	188.8 ± 75.1 (52-292)
Urinary urea (g/24 h)	32.6 ± 8.1 (21.4-42.3)	27.4 ± 7.1 (16-48.2)	29.8 ± 6.2 (14.6-38.3)	30.9 ± 9.7 (18.4-48.3)	24.3 ± 10.1 (8.4-39.8)	28.3 ± 15 (7.8-53)
Proteinuria (g/24 h)	2.8 ± 1.4 (1-6.6)	2 ± 1.5*† (0.5-7.7)	1.9 ± 1.4*† (0.3-6.4)	3 ± 2.2 (1-7.8)	3.1 ± 1.9 (1.2-6.8)	3.5 ± 2.1 (0.7-8.1)

Enrique Morales, *Kidney Dis* 41:319-327

N: 453,946
CKD; stage3-5

CKD Stage	BMI	Number of patients
3A	0-<20	6,247
3A	20-<25	60,548
3A	25-<30	127,020
3A	30-<35	75,827
3A	35-<40	27,043
3A	40-<45	8,460
3A	45-<50	2,725
3A	>=50	1,253
3B	0-<20	2,826
3B	20-<25	25,179
3B	25-<30	46,884
3B	30-<35	26,915
3B	35-<40	9,753
3B	40-<45	3,088
3B	45-<50	924
3B	>=50	445
4.0	0-<20	755
4.0	20-<25	6,193
4.0	25-<30	10,241
4.0	30-<35	5,804
4.0	35-<40	2,199
4.0	40-<45	678
4.0	45-<50	250
4.0	>=50	112
5.0	0-<20	88
5.0	20-<25	665
5.0	25-<30	971
5.0	30-<35	553
5.0	35-<40	191
5.0	40-<45	75
5.0	45-<50	25
5.0	>=50	9



Lu JL, *J Am Soc Nephrol*. 2014;25:2088-2096

N: 453,946
CKD; stage3-5

CKD Stage	BMI	Number of pat
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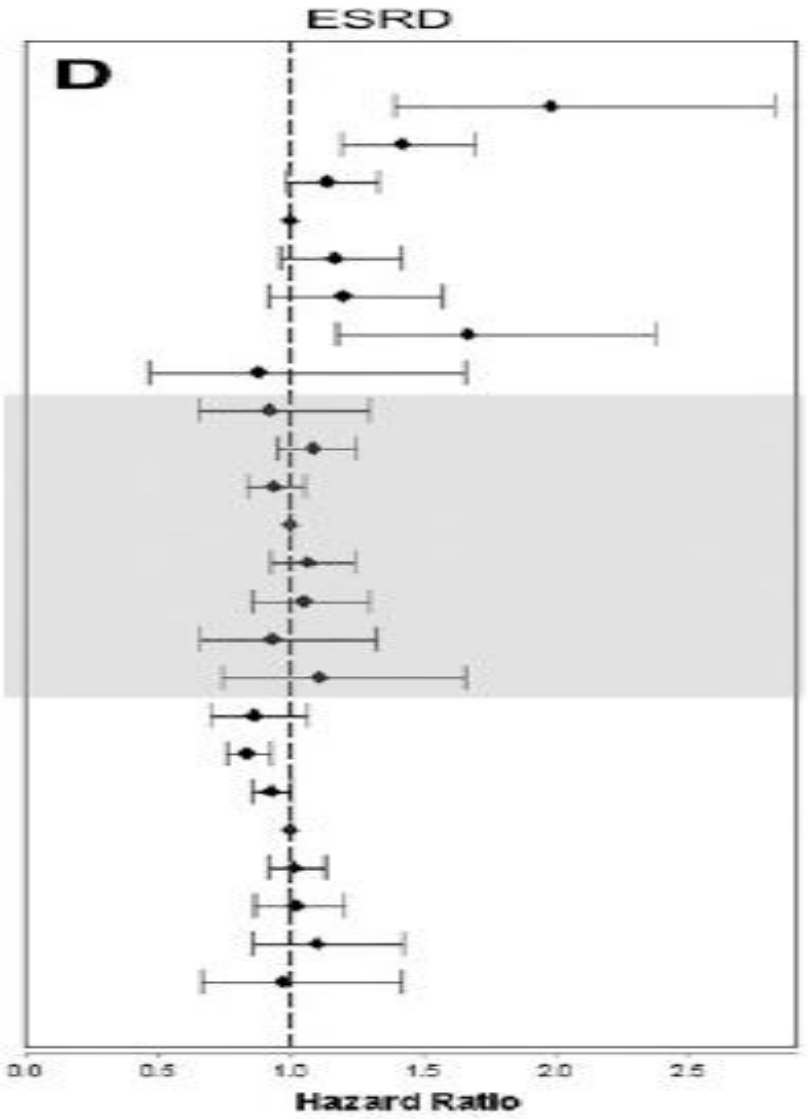
3A	35-<40	27,043
3A	40-<45	8,460
3A	45-<50	2,725
3A	>=50	1,253
3B	0-<20	2,826
3B	20-<25	25,179
3B	25-<30	46,884
3B	30-<35	26,915
3B	35-<40	9,753
3B	40-<45	3,088
3B	45-<50	924
3B	>=50	445
4.0	0-<20	755
4.0	20-<25	6,193
4.0	25-<30	10,241
4.0	30-<35	5,804
4.0	35-<40	2,199
4.0	40-<45	678
4.0	45-<50	250
4.0	>=50	112



N: 920
CKD; stage 4-5
Follow up: 4 yr

Table 2. Hazard Ratios From Cox Regression Models for Time to RRT in 920 Patients With CRF

	Crude Relative Risk	aRR*	95% CI
Age (y)			
<45	1.00	Reference	
45-64	0.99	0.95	0.78-1.17
≥65	0.77	0.72	0.57-0.90
Sex			
Female	1.00	Reference	
Male	1.32	1.59	1.35-1.88
BMI (kg/m^2)			
≤20	1.23	1.26	0.95-1.67
20.1-25	1.00	Reference	
25.1-30	0.81	0.79	0.67-0.94
>30	0.85	0.86	0.68-1.07
Primary renal disease			
Glomerulonephritis		Reference	
Diabetes	1.14	1.24	1.02-1.51
Hereditary disease	0.93	1.05	0.81-1.36
Nephrosclerosis	0.82	0.86	0.68-1.10
Other	0.77	0.79	0.63-0.99
GFR (mL/min)			
≥18.5	1.00	Reference	
16.7-18.4	0.89	1.20	0.96-1.50
13.7-16.6	1.11	1.52	1.21-1.91
<13.7	1.67	2.27	1.83-2.82
P for trend <0.0001			

Evans M, . Am J Kidney Dis. 2005; 46:863–870

N: 920
CKD; stage 4-5
Follow up: 4 yr

Table 3. Hazard Ratios From Cox Regression Models for Time to Death in 920 Patients With CRF

	Crude Relative Risk	aRR*	95% CI
Age (y)			
<45	1.00	Reference	
45-64	3.69	2.83	1.66-4.80
≥65	9.98	5.23	3.06-8.95
Sex			
Female	1.00	Reference	
Male	1.07	1.19	0.94-1.50
BMI (kg/m^2)			
≤20	1.49	1.96	1.35-2.84
20.1-25	1.00	Reference	
25.1-30	1.10	0.81	0.64-1.02
>30	0.95	0.70	0.51-0.97
Primary renal disease			
Glomerulonephritis	1.00	Reference	
Diabetes	3.55	3.13	2.25-4.34
Hereditary disease	0.70	1.14	0.64-2.03
Nephrosclerosis	2.50	1.56	1.08-2.27
Other	2.70	1.71	1.20-2.44

*Adjusted for age, sex, BMI, primary renal disease, GFR at inclusion, and transplantation during follow-up.

Evans M, . Am J Kidney Dis. 2005; 46:863–870

Hemodialysis patients

N: 418,055
HD: up to 5 yr
Follow-up: 2 yr

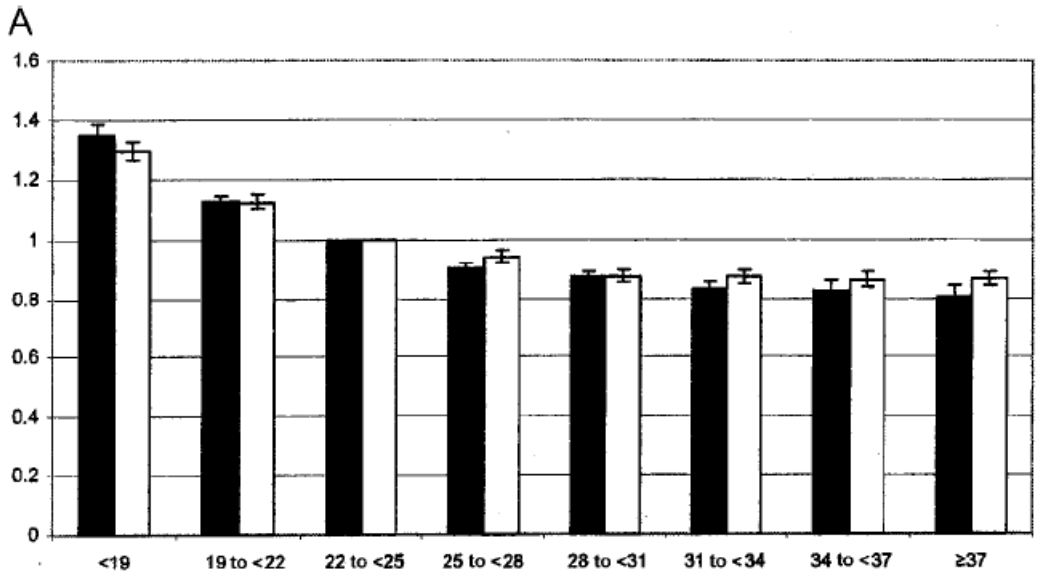
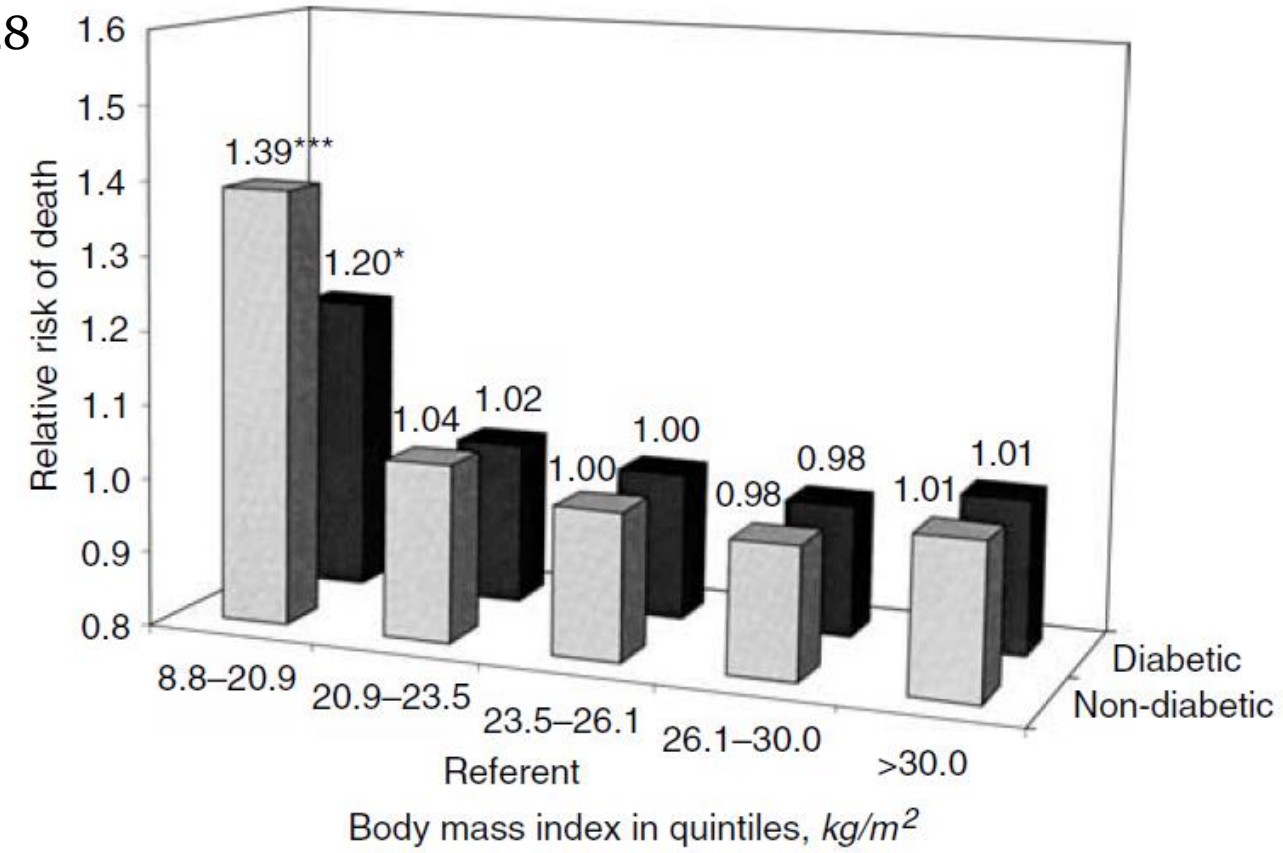


FIGURE1. Hazard ratios for death among men (▄) and women (□) by category of BMI.

Johansen KL, Am J Clin Nutr. 2004; 80:324–332

peritoneal dialysis patients

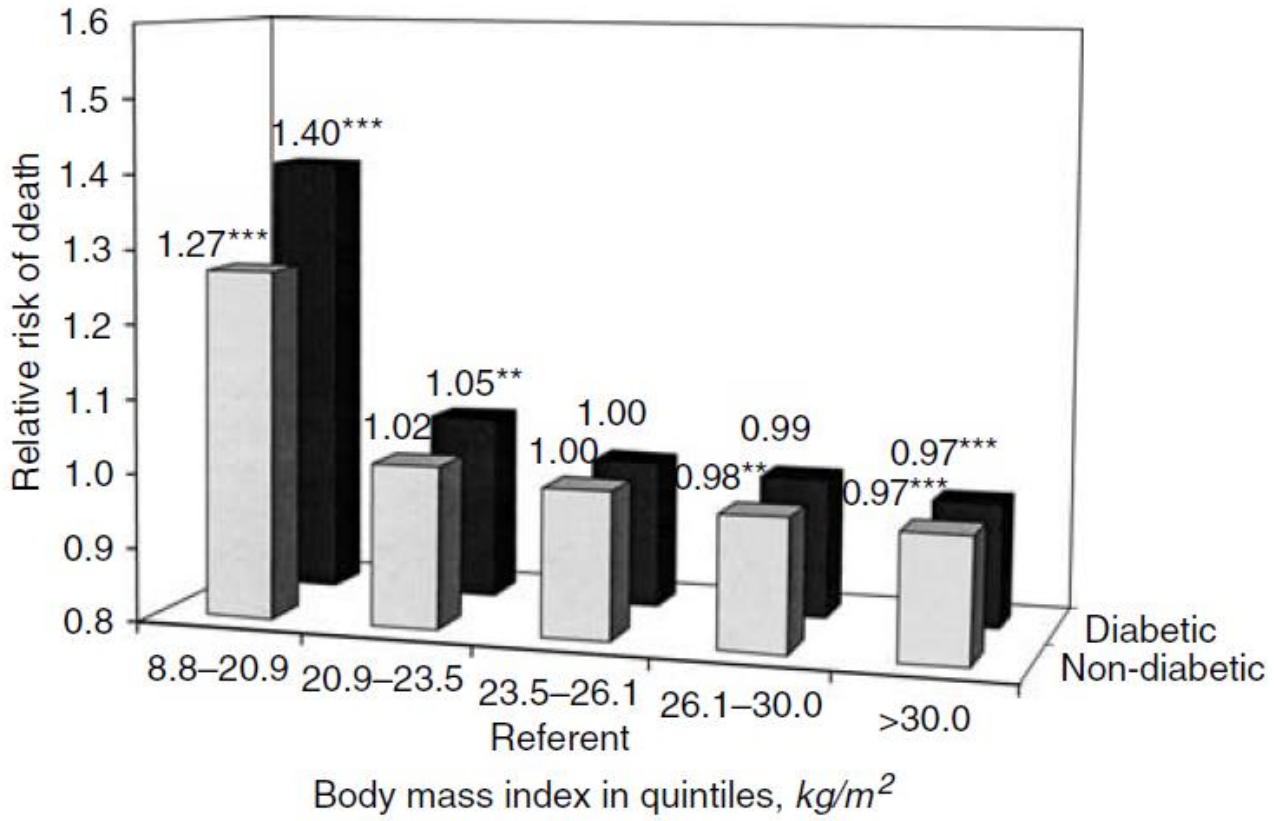
N: 134,728
PD: 13%



Relative risk of death by body mass index (BMI) quintile for new end-stage renal disease(ESRD)patients treated with peritoneal dialysis.

Stack AG, Kidney Int. 2004; 65:2398–2408.

N: 134,728
HD: 87%



Relative risk of death by body mass index (BMI) quintile for new end-stage renal disease (ESRD) patients treated with hemodialysis.

Stack AG, Kidney Int. 2004; 65:2398–2408.

Nephrol Dial Transplant (2013) 0: 1–17
doi: 10.1093/ndt/gft302

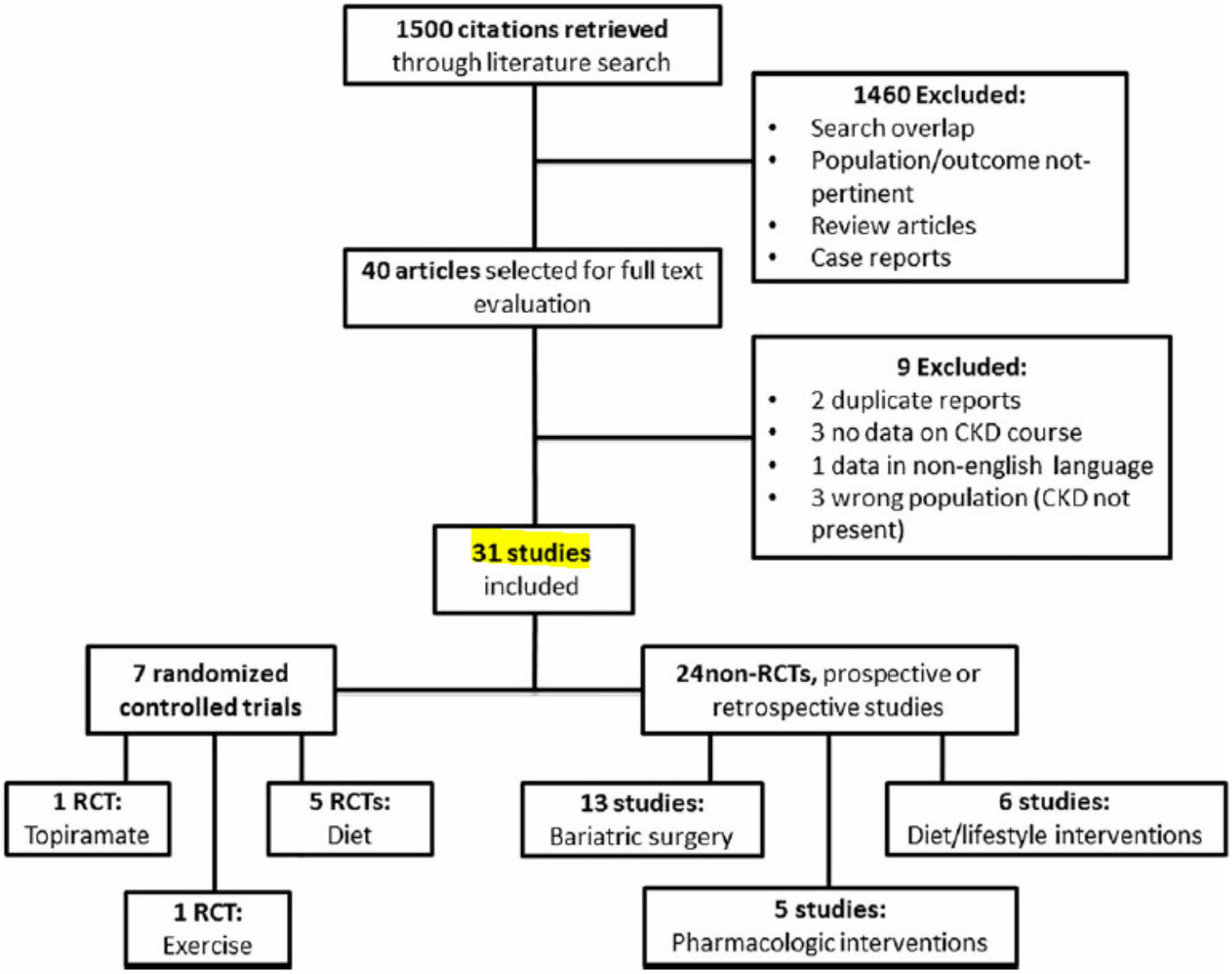
ndt
Nephrology Dialysis Transplantation

Full Review

Effects of weight loss on renal function in obese CKD patients: a systematic review

Davide Bolignano* and Carmine Zoccali

Clinical Epidemiology and Pathophysiology of Renal Diseases and Hypertension of Reggio Calabria, CNR-IBIM, Reggio Calabria, Italy


1500 citations retrieved through literature search
1460 Excluded:
• Search overlap
• Population/outcome not-pertinent
• Review articles
• Case reports
40 articles selected for full text evaluation
9 Excluded:
• 2 duplicate reports
• 3 no data on CKD course
• 1 data in non-english language
• 3 wrong population (CKD not present)
31 studies included
7 randomized controlled trials
24non-RCTs, prospective or retrospective studies
1 RCT: Topiramate
5 RCTs: Diet
1 RCT: Exercise
13 studies: Bariatric surgery
6 studies: Diet/lifestyle interventions
5 studies: Pharmacologic interventions

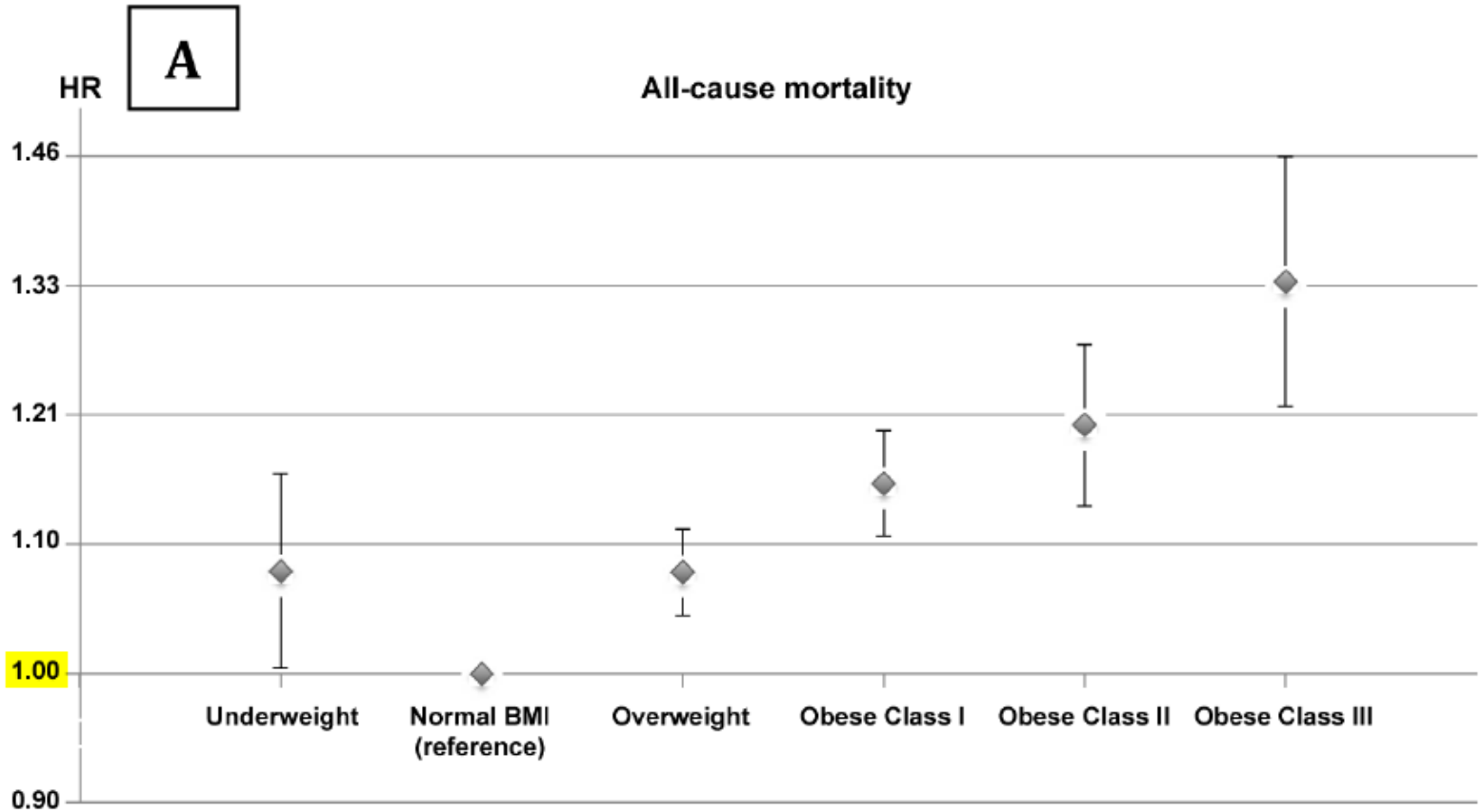
Baseline alterations in renal Function included:

- Hyperfiltration
- Pathological albuminuria
- Overt CKD
- HD

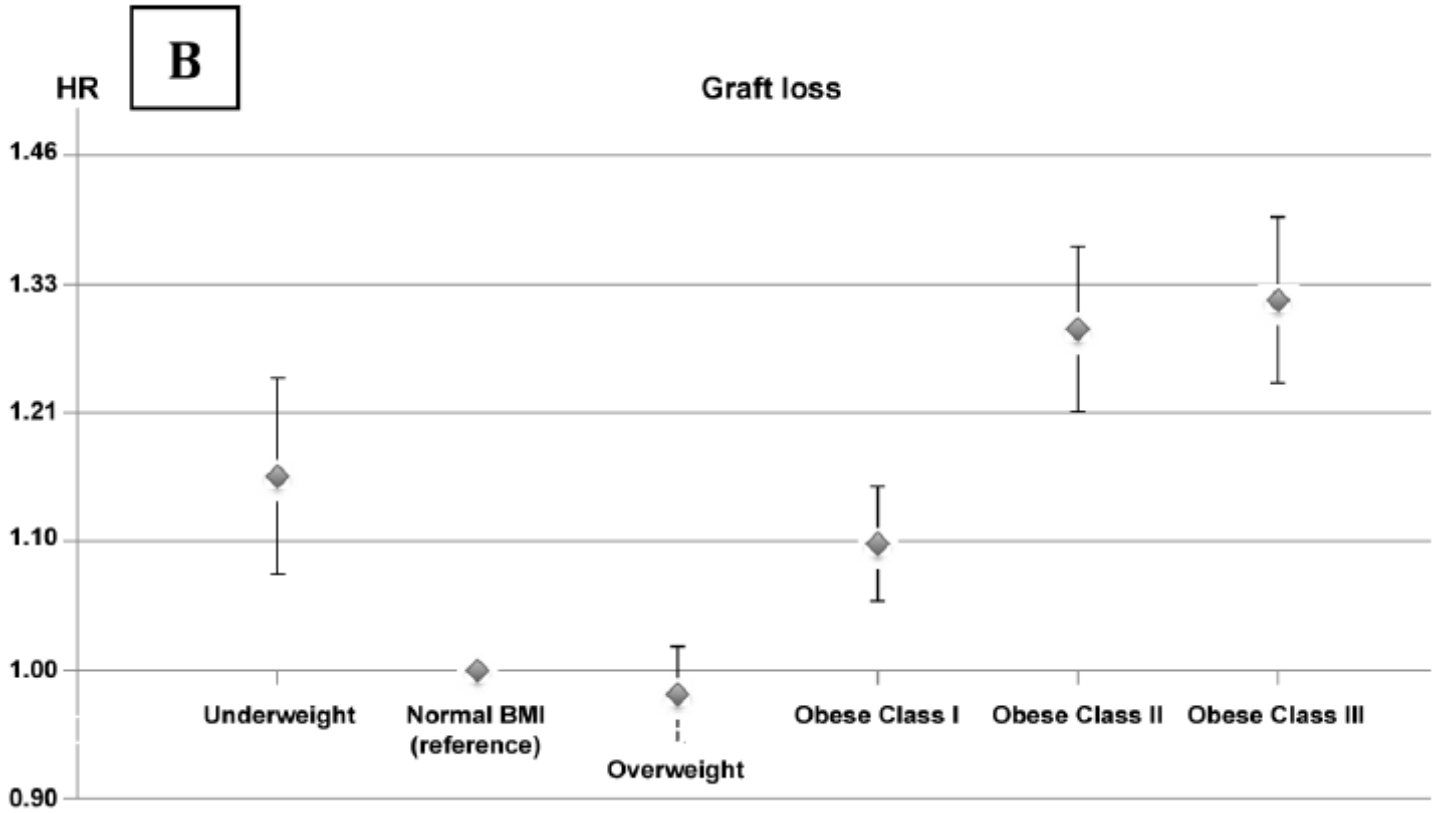
Non-surgical intervention leads to:

- Short-term weight reduction
- Improvements in BP, lipide profile, and proteinuria
- Diffèrent pattern of change in GFR

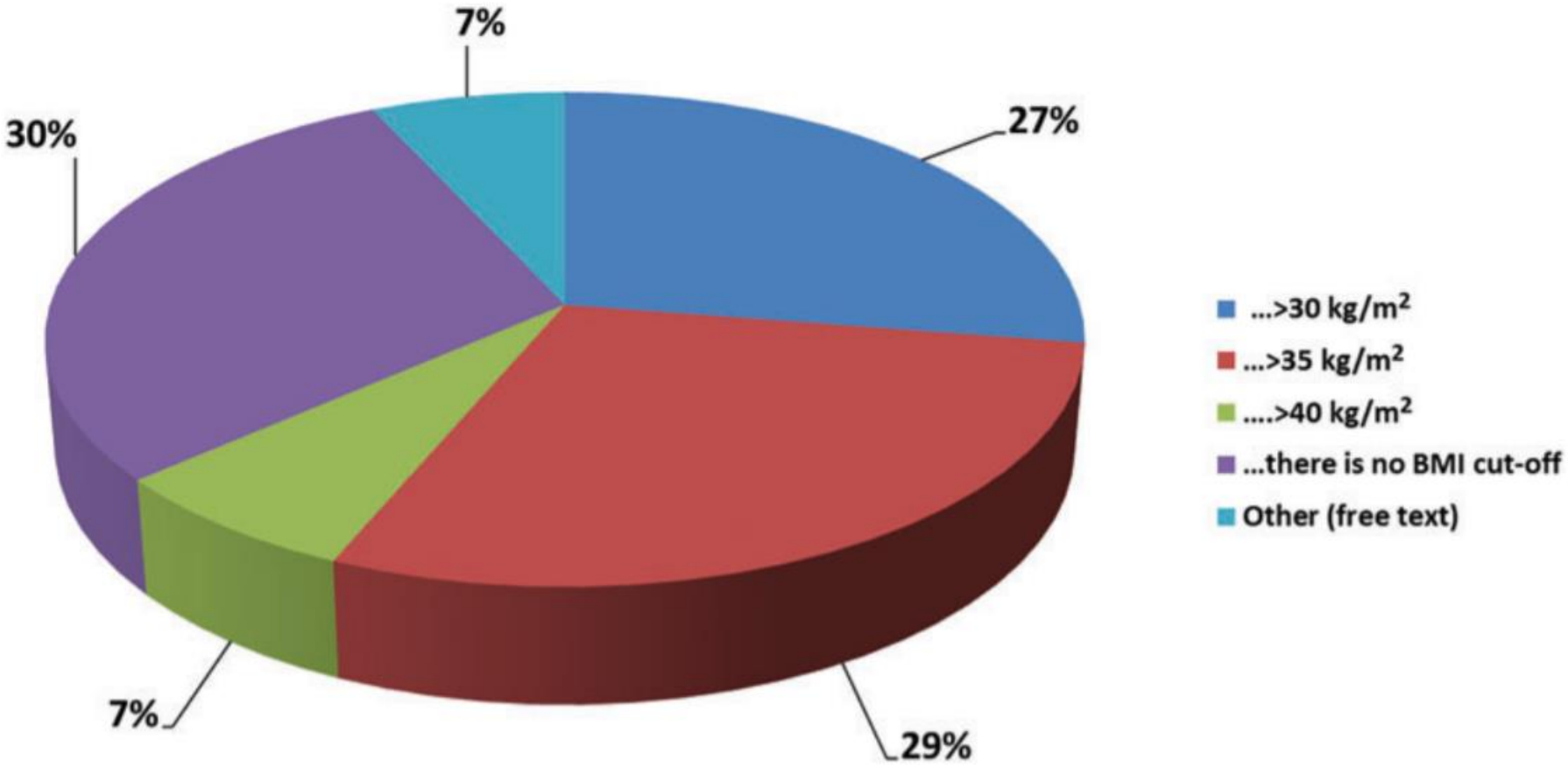
kidney transplant candidates



Revealed the adjusted HRs of 'all-cause mortality'.



Revealed the adjusted HRs ‘graft failure’



Peter Stenvinkel, et al, Nephrol Dial Transplant (2013) 28 (Suppl. 4): iv99–iv104

kidney transplant recipients

Approximately one-third of post-transplant patients gain weight due to:

- Increased appetite
- Less dietary restriction due to normalization of renal function
- Initial inactivity following surgery
- General well-being post transplantation
- Medications such as steroids

N: 292
Follow up: 1yr

Post-Transplant Weight Gain and Graft Loss

Table 4: Cox model: hazard ratio estimates graft loss and 95% confidence intervals (model 2)

Variable	Category	Hazard ratio	95% CI	p-value
Creatinine clearance (mL/min)	≥50	1	—	—
	<50	4.72	[1.63; 13.69]	0.004
Urinary protein excretion (g/day)	<0.5	1		
	≥0.5	3.21	[1.27; 8.18]	0.014
Variation in BMI (%)	≤5	1	—	—
	>5	2.82	[1.11; 7.44]	0.015
Metabolic syndrome	Absent	1	—	—
	Present	1.65	[0.69; 4.22]	0.31
Delayed graft function	No	1	—	—
	Yes	2.61	[1.07; 6.39]	0.036
Low-grade inflammation (mg/L)	CRP < 3	1	—	—
	CRP ≥ 3	2.02	[0.84; 5.12]	0.10

D. Ducloux, et al, American Journal of Transplantation 2005; 5: 2922–2928

Who is appropriate candidate for weight loss therapy?

Weight management strategies for those with chronic kidney disease – a consensus report from the Asia Pacific Society of Nephrology and Australia and New Zealand Society of Nephrology 2016 renal dietitians meeting

Short title: Weight management consensus report

Corresponding author details:

- Weight loss in obese adults who have **mild to moderate CKD** results in a significant decrease in proteinuria and albuminuria, **irrespective of the weight loss strategy** applied.

- There is **no strong recommendation** for weight loss in patient with **severe CKD**.

- There is **inadequate evidence** to support intentional weight loss in overweight or obese **kidney transplant candidates.**

- To **prevent excessive weight gain,** Kidney transplant recipients should be referred to a **dietitian** as soon as practicable after transplantation, for preventing weight gain.
- Following kidney transplantation, **maintain ideal body weight** by **healthy diets** and **regular exercise.**
- **Orlistat** can lead to sub-therapeutic immunosuppressive levels.
- **Consider bariatric surgery** for the morbidly obese patient who has been unable to lose weight by these means, and especially in the presence of HTN, DM and sleep apnea.

Steven Chadban, Transplantation Nutrition, 2010 Asian Pacific Society of Nephrology. Brian Camilleri, et al, Transplant Rev 2016; 30: 203-211

summary

Mild-moderate CKD	Benefit from weight loss with any strategy.
Severe CKD (HD)	No obvious benefit (obesity paradox)
Candidate for kidney transplant	Individualized (BMI: 30-35 kg/m^2 associated with best results)
Kidney recipients	Benefit from weight loss (lifestyle intervention and bariatric surgery)

Preferred weight loss medication: individualization of therapy

preferred drug **with caution** **avoid**

	Orlistat	lorcaserin	Phentermin/ topiramate	Naltroxen/ bupropione	Liraglutide 3 mg
Mild CKD					
Moderate CKD			Dose adjustment	Dose adjustment	
Severe CKD (HD)	Monitor for oxalat nephropathy				Avoid vomiting dehydration
Kidney recipients					
Nephrolithiasis	Ca oxalate stone		Ca phosphate stone		

AACE/ACE Obesity CPG, *Endocr Pract.* 2016;22

The **ideal BMI** and the **best ways to achieve this BMI** need to be established in CKD patients.