The Impact of Obesity on Dialysis and Transplant Management: The Adult Experience

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Disclosures

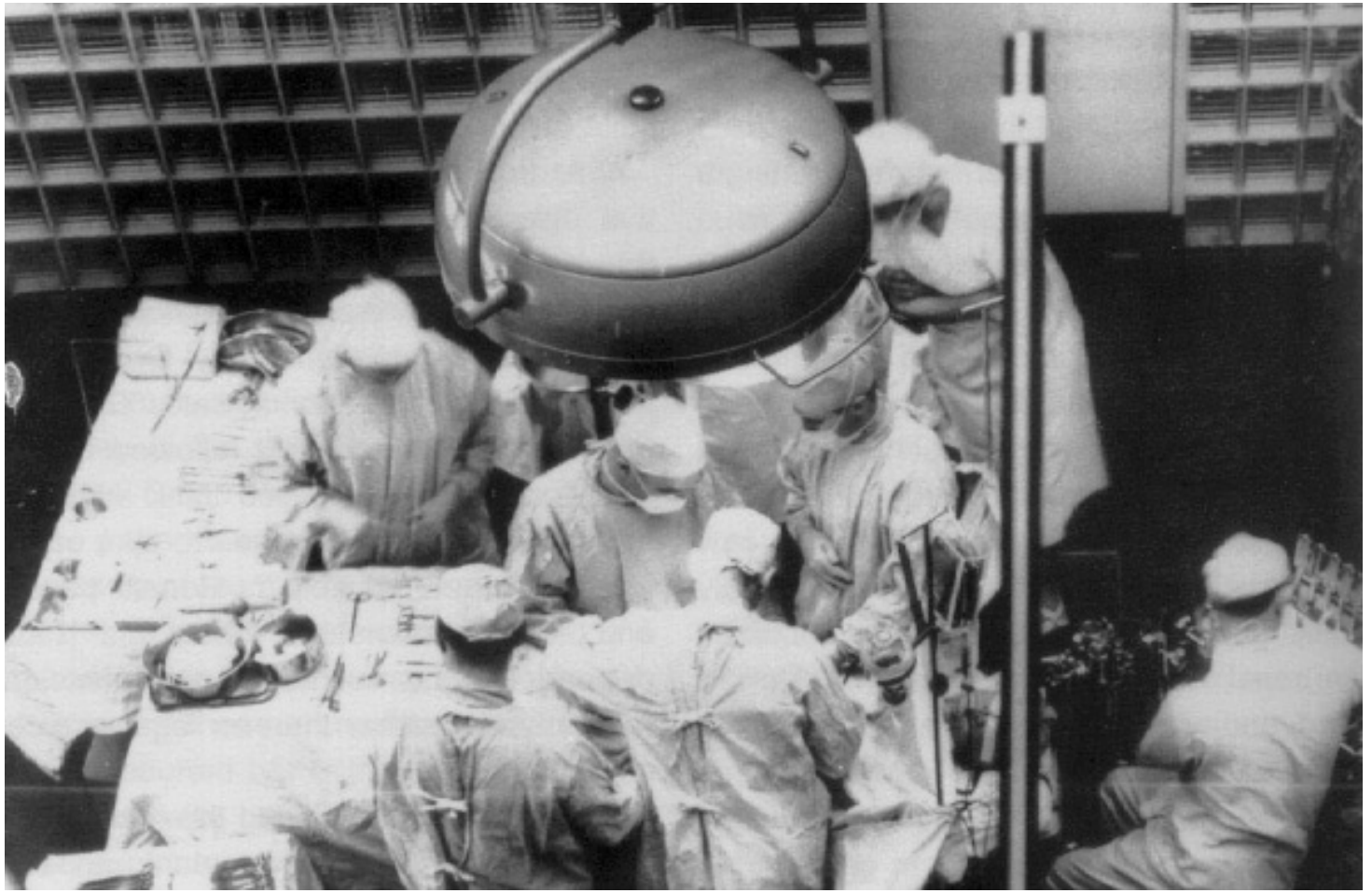
- **Advisory Board:**
  - CareDx
- **Speaker's Bureau:**
  - Mallinckrodt Pharma
  - Veloxis Pharma
- **Scientific Support:**
  - Pfizer
  - Novartis
  - Dept of Defense
  - CareDx

- **Conflict of Interest: None relevant for this talk**

Objectives

- Recognize the burden of kidney disease in US
- Understanding the scope of the problem and barriers for transplant with Morbid Obesity in ESKD patient
- UC TRIMS/Weight loss program-process and outcomes

1st Successful Kidney Transplant



Joseph Murray and the medical team at Boston's Peter Bent Brigham Hospital perform the first successful long-term organ transplant, Dec. 23, 1954

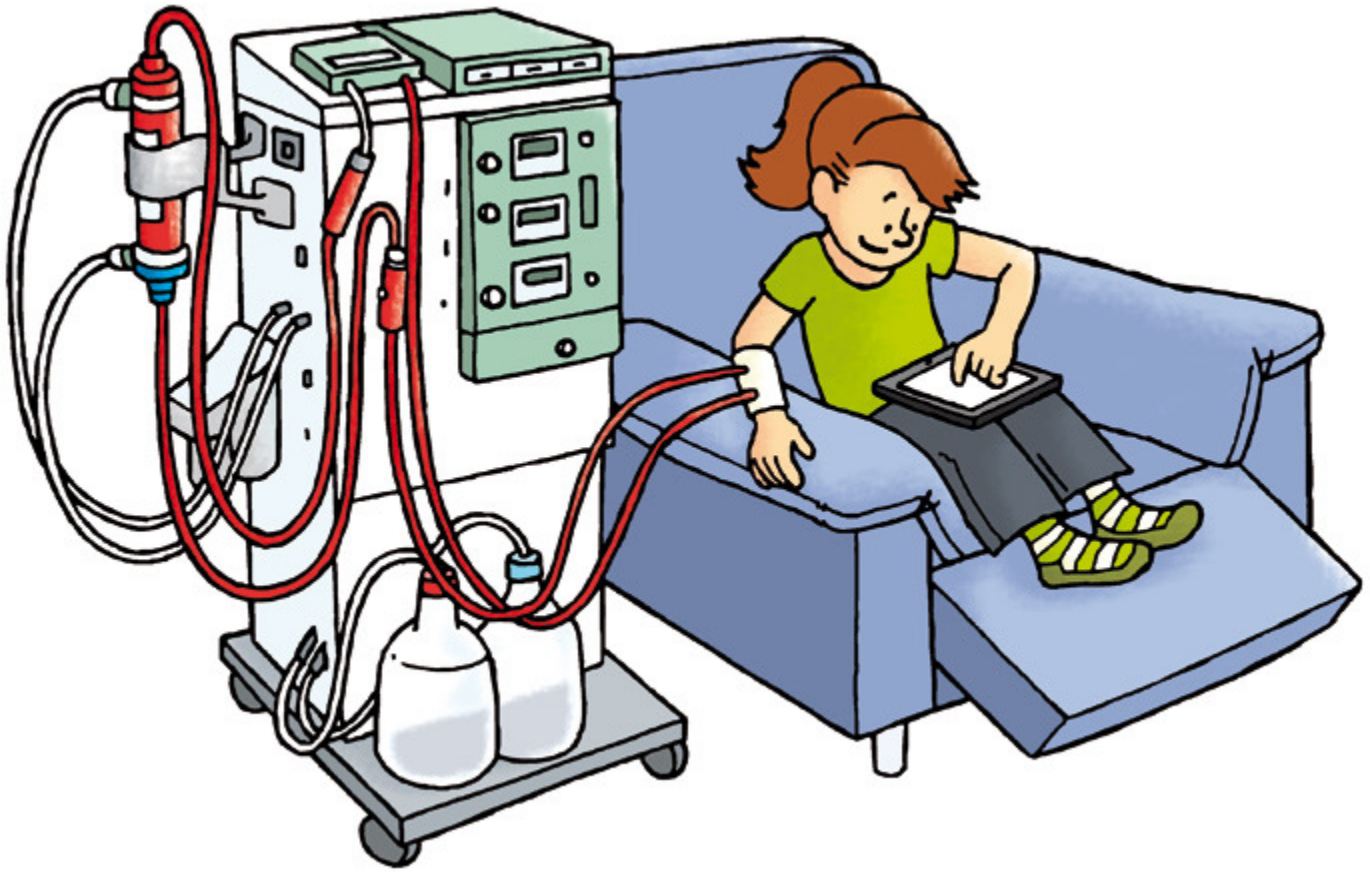
Burden of Kidney Disease in US

- 37 million patients have chronic kidney disease
- >726,000 have end-stage kidney disease (ESKD)
- Kidney disease ranks as the ninth leading cause of death in America
- Approx. 20% of dollars in traditional Medicare—$114 billion a year—spent on kidney disease
- Yet for > 100,000 Americans who begin dialysis to treat end-stage kidney disease each year, one in five will die within a year

Case History

- JB 28 yr old WF ESKD d/t IgA Nephropathy
- On HD for 2 years
- Blood group O, cPRA 0%
- BMI 43
- Has few potential living donors
- Declined for transplant as BMI over the cut-off for most transplant centers

“I’m tired of waiting…”



The Solution

- **Kidney Transplantation**

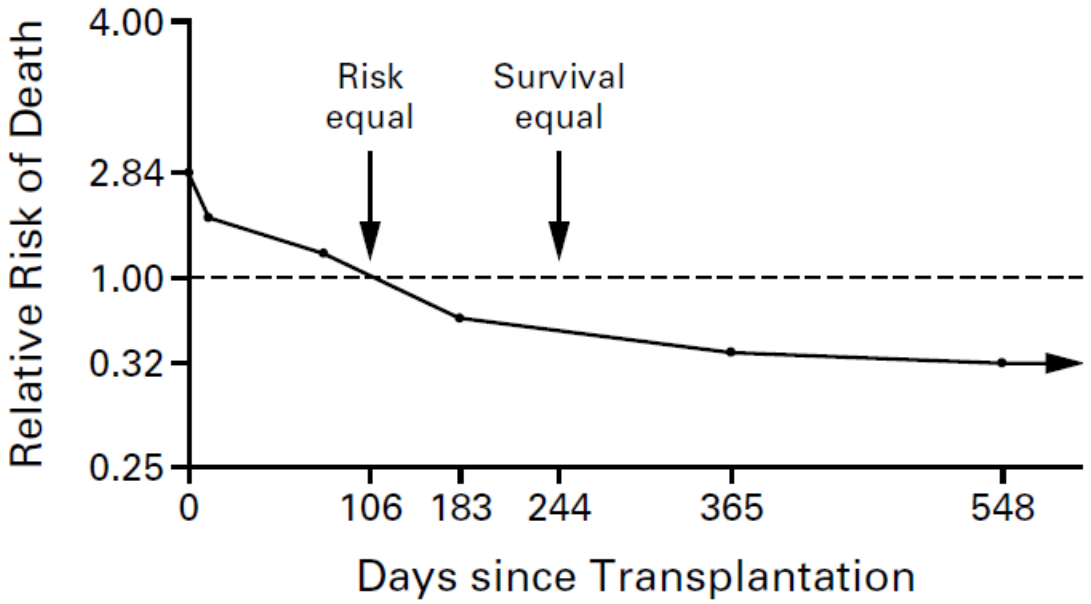
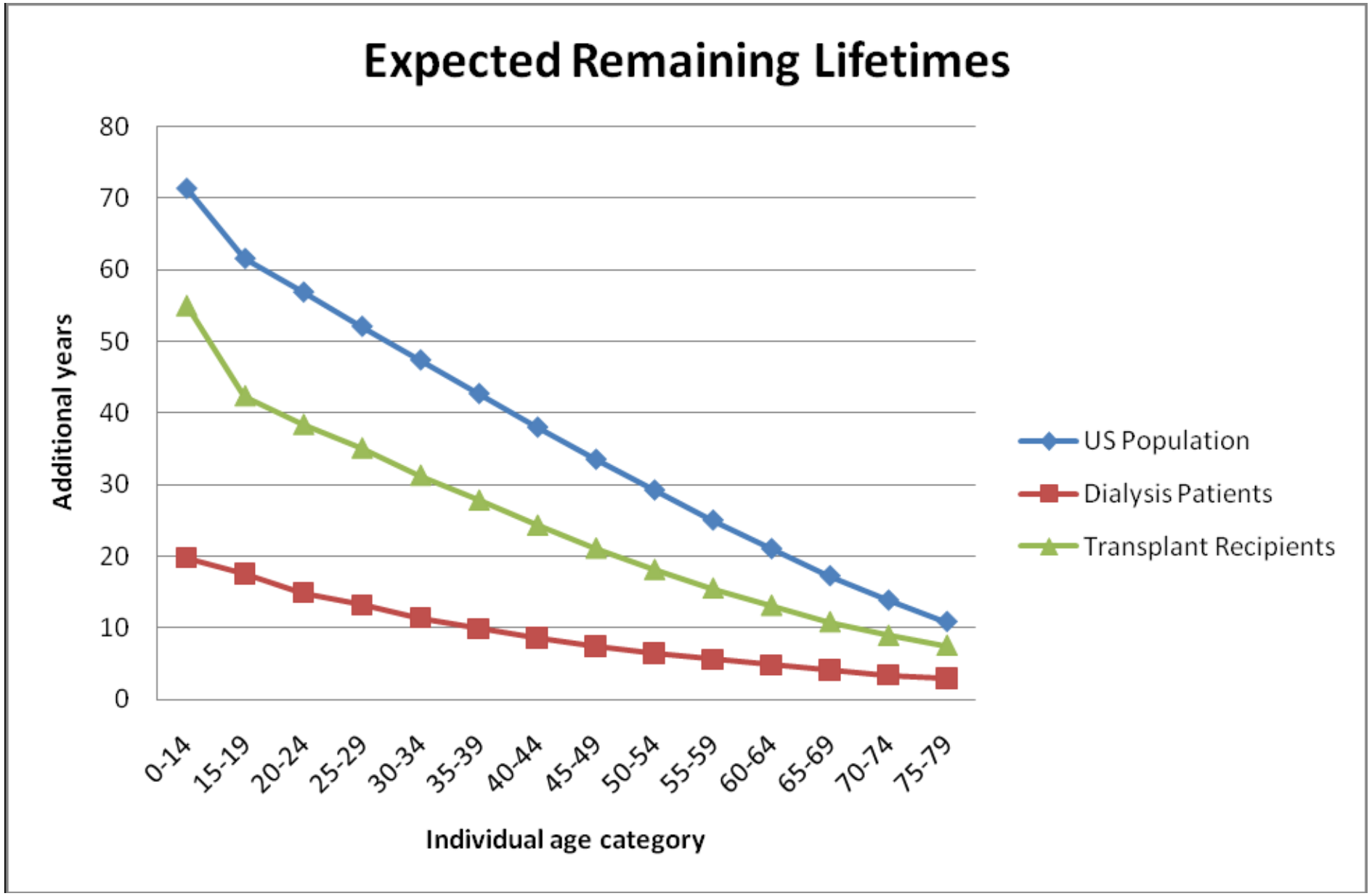


Figure 2. Adjusted Relative Risk of Death among 23,275 Recipients of a First Cadaveric Transplant.

N Engl J Med 1999;341:1725-30



2022 UNOS Data for Kidney Transplant

- **Kidney Transplants: 25,498**
- **-Living: 5,863 (23%)**

  -Deceased: 19,635 (77%)

- **Kidney Waitlist candidates: 96,502**

  (OPTN data- Jan 19th,2022 12:00 AM)

Current demand for kidney allografts exceeds available supply

UC Health

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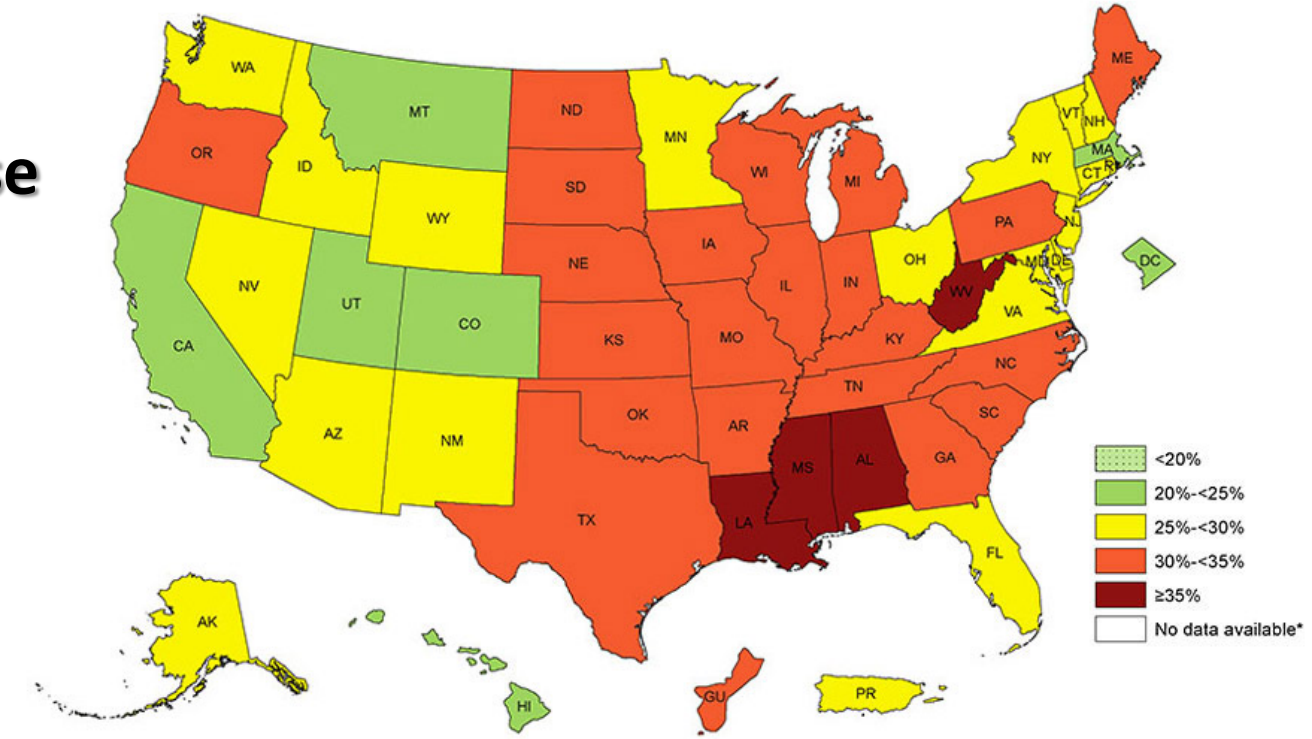
Prevalence of Obesity in US

36.5% US adults are obese (BMI>30)



60% of patients undergoing kidney transplant have BMI >30

1. Ogden CL, Carroll MD, Fryar CD, Flegal KM. Prevalence of obesity among adults and youth: United States, 2011–2014. NCHS data brief, no 219. Hyattsville, MD: National Center for Health Statistics. 2015.

Challenges of Obesity for ESKD patients

- Difficulties in creating vascular access and inserting Tenckhoff catheters
- Higher rates of catheter malfunction and peritonitis
- Need for longer and/or more frequent dialysis (or peritoneal dialysis [PD] exchanges) to achieve adequate clearance
- Increased metabolic complications particularly with PD
- Obesity is a barrier to kidney transplantation:
  - BMI >40 kg/m2 is contraindication to transplant at most centers (most centers prefer BMI <35 or 38)
  - Obesity is third most common reason to be on hold on the waitlist

Obesity Paradox

- Paradoxically, obesity has been associated with improved survival in the hemodialysis population
- While a normal or low BMI is associated with worse outcomes

Obesity Paradox

- overweight (BMI 25–30, *n*=2541)
- mild (grade I) obesity (BMI 30–35, *n*=1054)
- moderate (BMI 35–40, *n*=355) and severe (BMI >40, *n*=153) obesity.

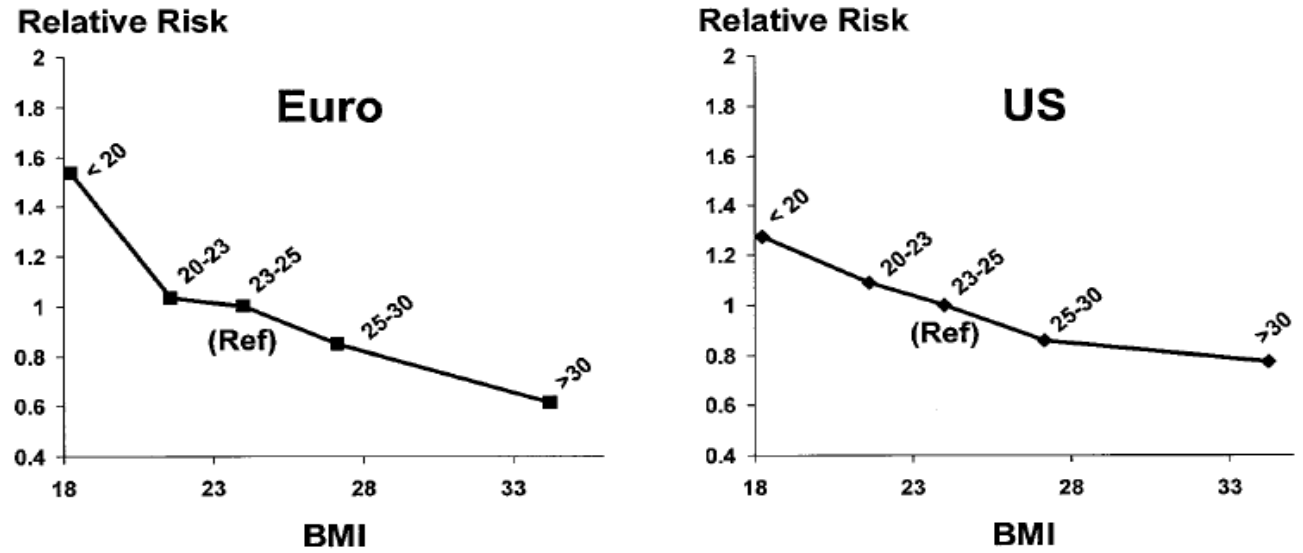
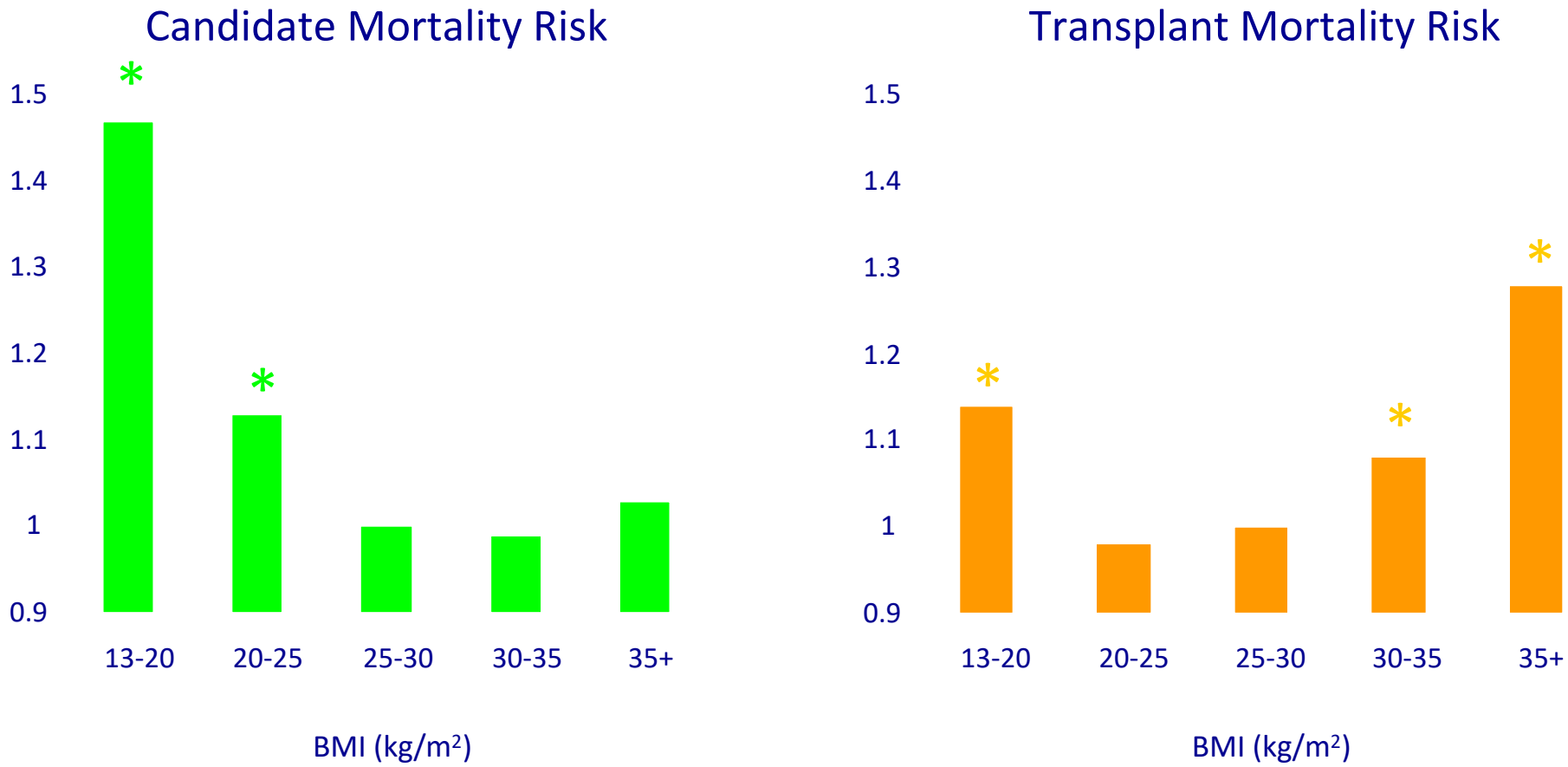


Fig. 2. Relative mortality risk *vs* BMI, US and Europe. BMI points from categorical analysis are plotted at the average BMI for each group. Mortality risk decreases as BMI increases. An inverse linear relationship between mortality and lnBMI is significant for both the US and Europe ($P < 0.0001$). Adjusted for demographics, all comorbid conditions listed in Table 1 and albumin.

Leavey SF, et al. Body mass index and mortality in 'healthier' as compared with 'sicker' hemodialysis patients: results from the Dialysis Outcomes and Practice Patterns Study (DOPPS) Nephrol Dial Transplant. 2001;16(12):2386–2394.

Obesity Paradox contd.



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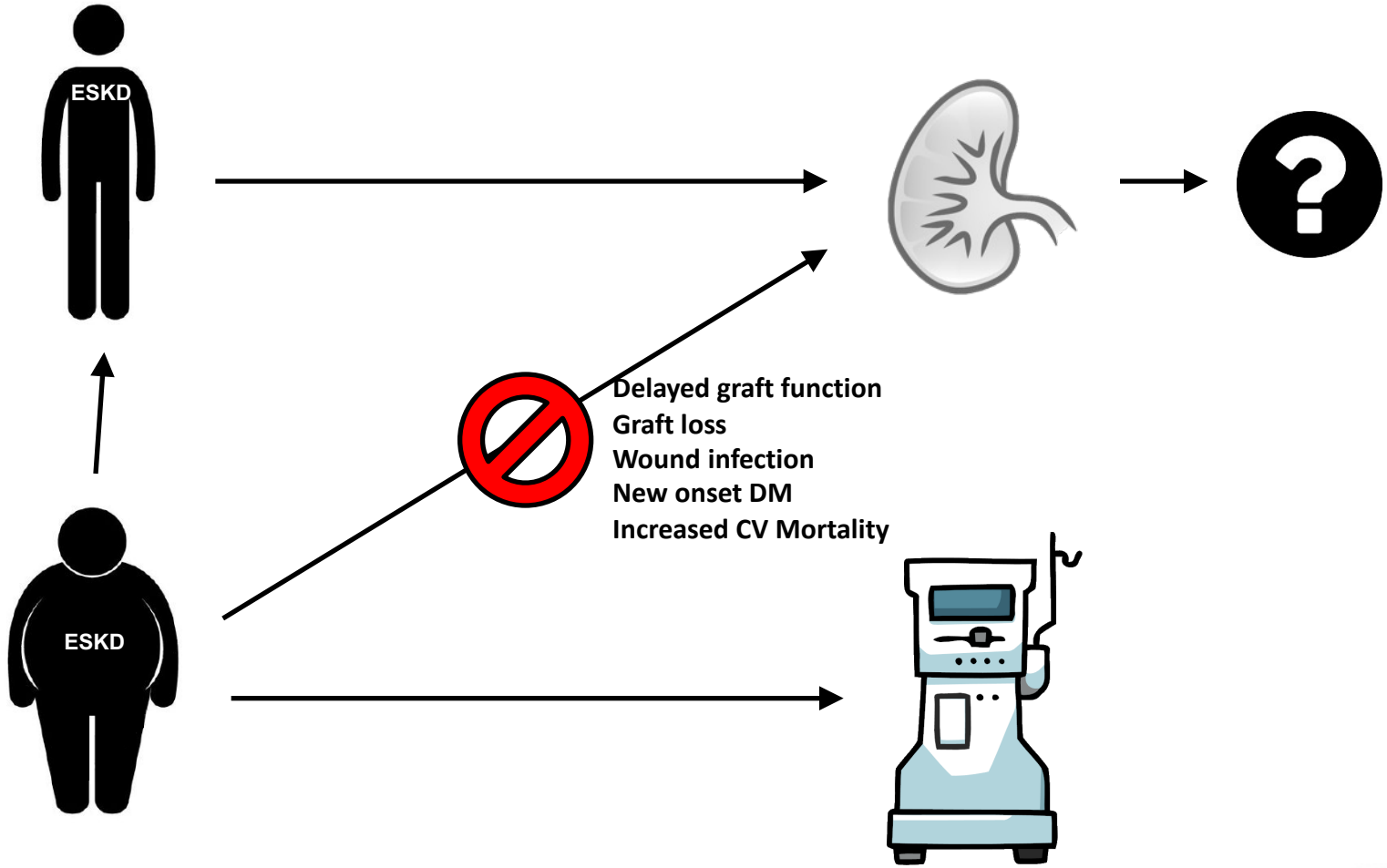
Theories for Obesity Paradox

- Protein-energy wasting and inflammation in patients with low BMI
- Competing risks- the dialysis survival may not be long enough to ascertain the overriding factors related to obesity associated cardiovascular processes like better tolerance of fluid shifts during hemodialysis leading to less intradialytic hypotension and ischemia
- Confounding by comorbidities- a low BMI is associated with more severe comorbidities that predispose to death
- Survivor bias - obese patients reaching ESKD are an atypical and minute fraction of the much larger population who died prior to ESKD because obesity is truly associated with early death (just as in the non-dialysis population
- Adipose tissue sequesters uremic toxins

Morbid Obesity: Scope of the problem

Prevalence of Obesity (BMI ≥30 kg/m2) in general population ~40%
Prevalence of Obesity in patients undergoing kidney transplantation ~60%



Impact of BMI on CKD and ESRD

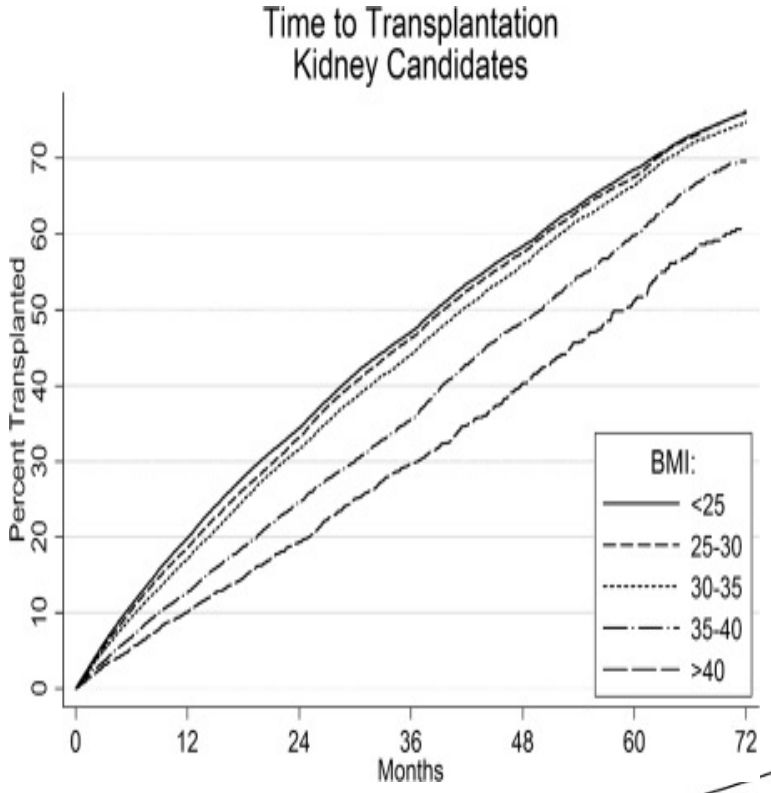
- Wound infection and healing impaired with BMI > 35.
- Relative risk of death-censored graft loss, cardiovascular death and infectious death increased by 1.8 fold with BMI > 36.
- Survival at 5 yrs 89% BMI < 30 vs 67% BMI > 30.

Meier-Kriesche, Transplantation, Vol 73(1) 2002

Access- Kidney

Data from UNOS 132,353 pts (1995-2006)

BMI	Time to Txp	Likelihood of Txp
25-30 (34.3%)	40 mon	Down 2-4%
31-35 (19.3%)	42 mon	Down 2-7%
36-40 (7.2%)	51 mon	Down 24-28%
>40 (2.7%)	59 mon	Down 42-44%



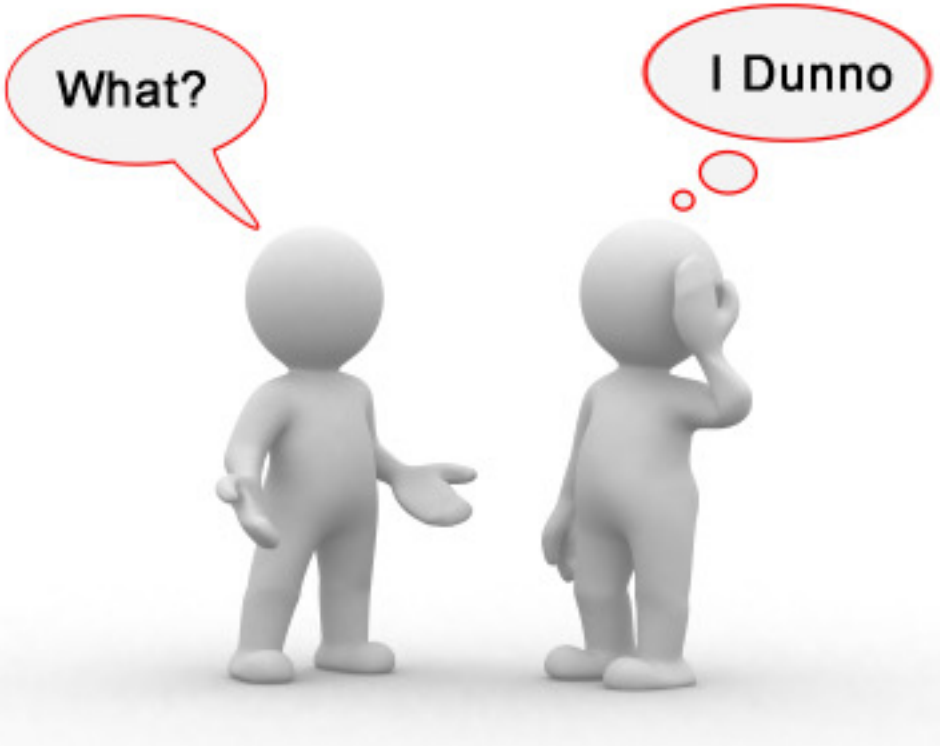
Obesity is third most common reason to be on hold on the waitlist

Segev et al, J Am Soc Nephrol. Dec 19, 2007.

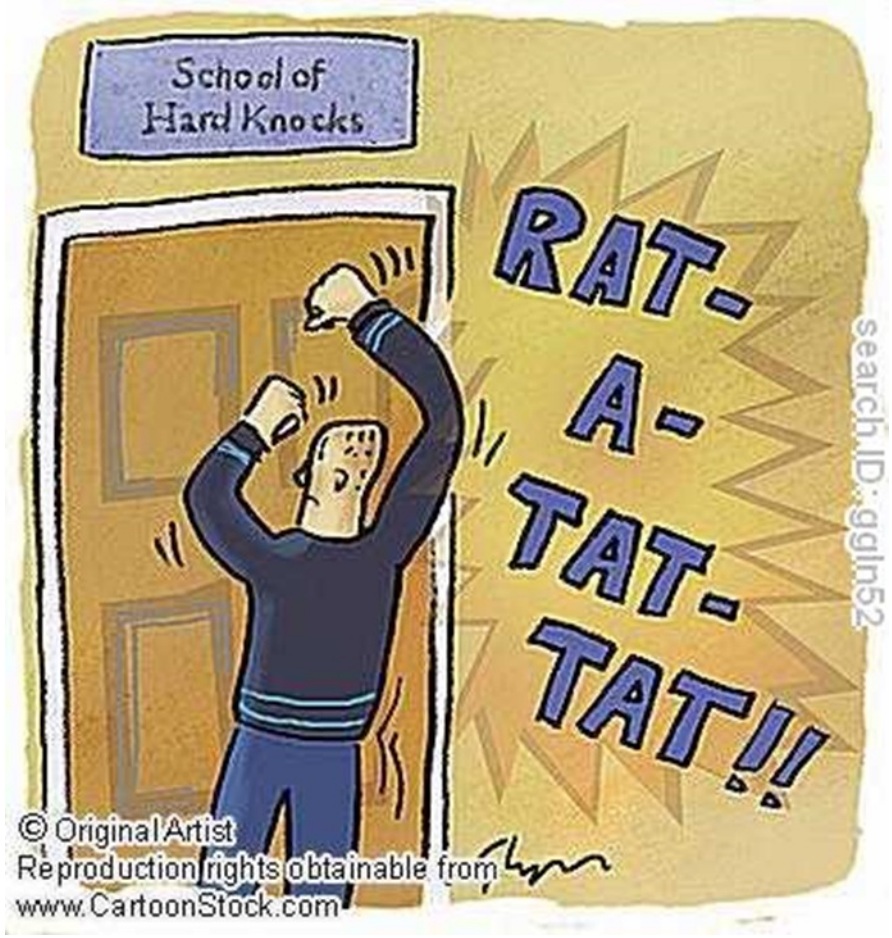
Evaluation of High BMI Patients - Past

Minimal guidance given for weight loss

Arbitrary time frame for weight loss



BMI as a barrier for transplant



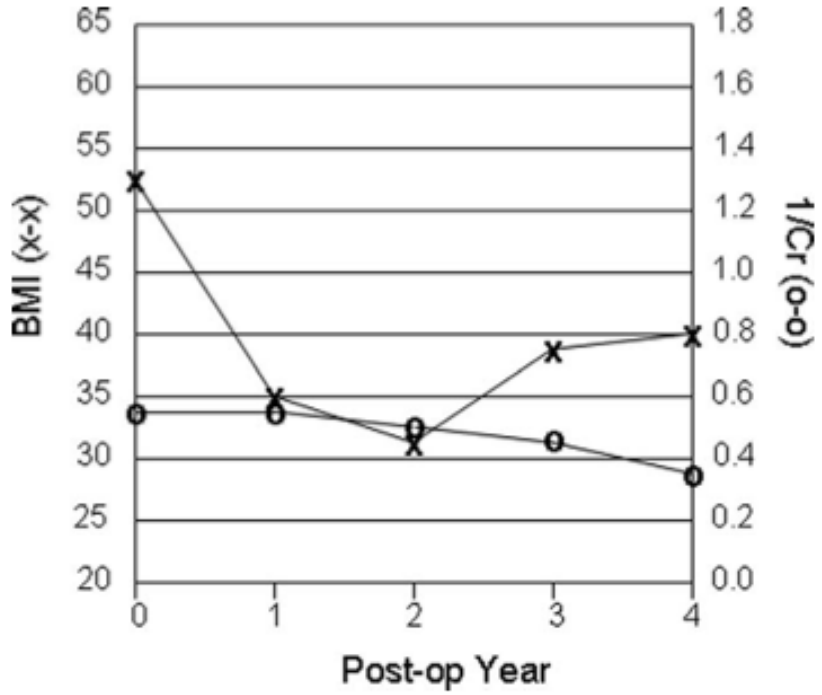
Prior UC Experience- 2009

Improvement and stabilization of chronic kidney disease after gastric bypass

J. Wesley Alexander, M.D., Sc.D.[a,*], Hope R. Goodman, M.P.T.[a], Lisa R. Martin Hawver, M.D.[a], Michael A. Cardi, M.D.[b]

[a]*Center for Surgical Weight Loss, Department of Surgery, University of Cincinnati College of Medicine, Cincinnati, Ohio*
[b]*The Kidney Hypertension Center, Cincinnati, Ohio*

- 45 nontransplant patients with renal disease
  - Mean BMI 48.9 ± 1.9kg/m^2
  - 14 went on to transplant
  - 31 remained on waitlist
- 31 patients on waitlist
  - 9 had evidence of stabilization or improvement in renal function
  - 2 patients on dialysis prior came off dialysis for 27 and 7 months, respectively

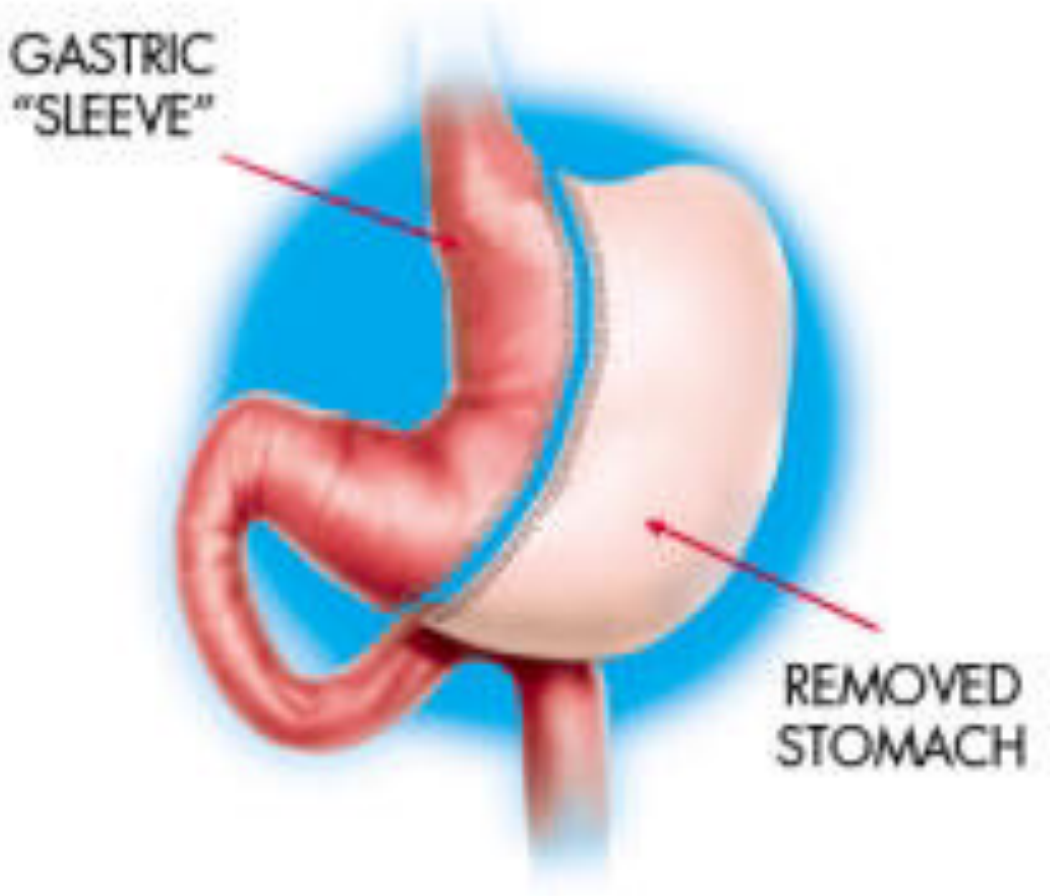


Surg Obes Relat Dis. 2009 Mar-Apr;5(2):237-41. doi: 10.1016/j.soard.2008.08.016. Epub 2008 Aug 27. PMID: 18996757.

Laparoscopic Sleeve Gastrectomy

Stapling device used by surgeon

- to divide stomach and create a small stomach the size
- of a banana
- Remaining 80% of stomach removed



Why Sleeve Gastrectomy?

	Roux-en-Y gastric bypass	BPD/DS	Sleeve Gastrectomy	Lap Band
Safety Mortality Morbidity	Death, deficiencies 0.3% 20%	Death, malnutrition 1% > 40%	Leak Stricture 0.2% <8%	Slipped band Erosion <0.1% >40%
Effectiveness EWL DM2 Resolution	> 60% at 5 years 84%	> 75% at 10 years 98%	> 60% at 4 years > 60%	> 40% at 4 years 48%
Revision Rate	13%	4%	7 - 20%	30 - 60%
Failure Rate (< 25%EWL)	2.5% at 10 years	6%	Up to 25%	Up to 40%

TRIMS: The initial UC Experience

- Specialized, multidisciplinary **TRIMS** (**transplant-related interdisciplinary metabolic surgery**) clinic
  - Bariatric/transplant surgeon
  - Transplant pharmacy
  - Transplant nephrology
  - Kidney team dietician
  - Exercise therapist

Process of TRIMS

- **Referral process**
  - Any person with BMI 35-39 with 2 comorbidities (HTN,OSA,DM2,HLD)
  - Or BMI > 40
- **Evaluation**
  - Appointment with Surgeon, Nurse and Dietitian
- **Testing**
  - 6 months consecutive visits with Dietitian/MD
  - EGD
  - Psychological clearance
  - Sleep study
  - Stress test
  - CXR
  - PFT
- **Insurance**
- **Preoperative**

Nutrition visits prior to surgery

- Initial RD and monthly nutrition visits prior to surgery:
  - Dietary Patterns
  - Medical Co-morbidities
  - Laboratory values
  - Weight History
  - Lifestyle factors
  - Readiness to change
  - Exercise Habits
  - Support System
  - Behavioral, cultural, psychosocial and economic issues

Preoperative diet

- Weight loss of 20-30 pounds prior to gastric sleeve improves outcomes
- Balanced calorie controlled diet initiated to achieve desired weight loss
  - Renal diet continues if HD
- Two weeks prior to surgery patients given “Pre-op” diet

Length of time	7 days (14 days prior)	7 days
Diet	Full liquid + Protein supplement	Clear liquid + Protein supplement
Recommended nutrient intake	1200 calories 90 grams protein	1000-1200 calories 90 grams protein
Foods to avoid	High fat Concentrated carb	Cream soups Milk
Sample foods	Boost Glucose Control (1 x/d) Low fat soy milk Cream of wheat Pureed oatmeal Pureed soups Any clear liquids	Powdered whey protein supplement Sugar free popsicles Sugar Free Jello Crystal light Low Sodium Chicken/Beef Broth Coffee-black Tea (sugar free)

Pre-operative Concerns

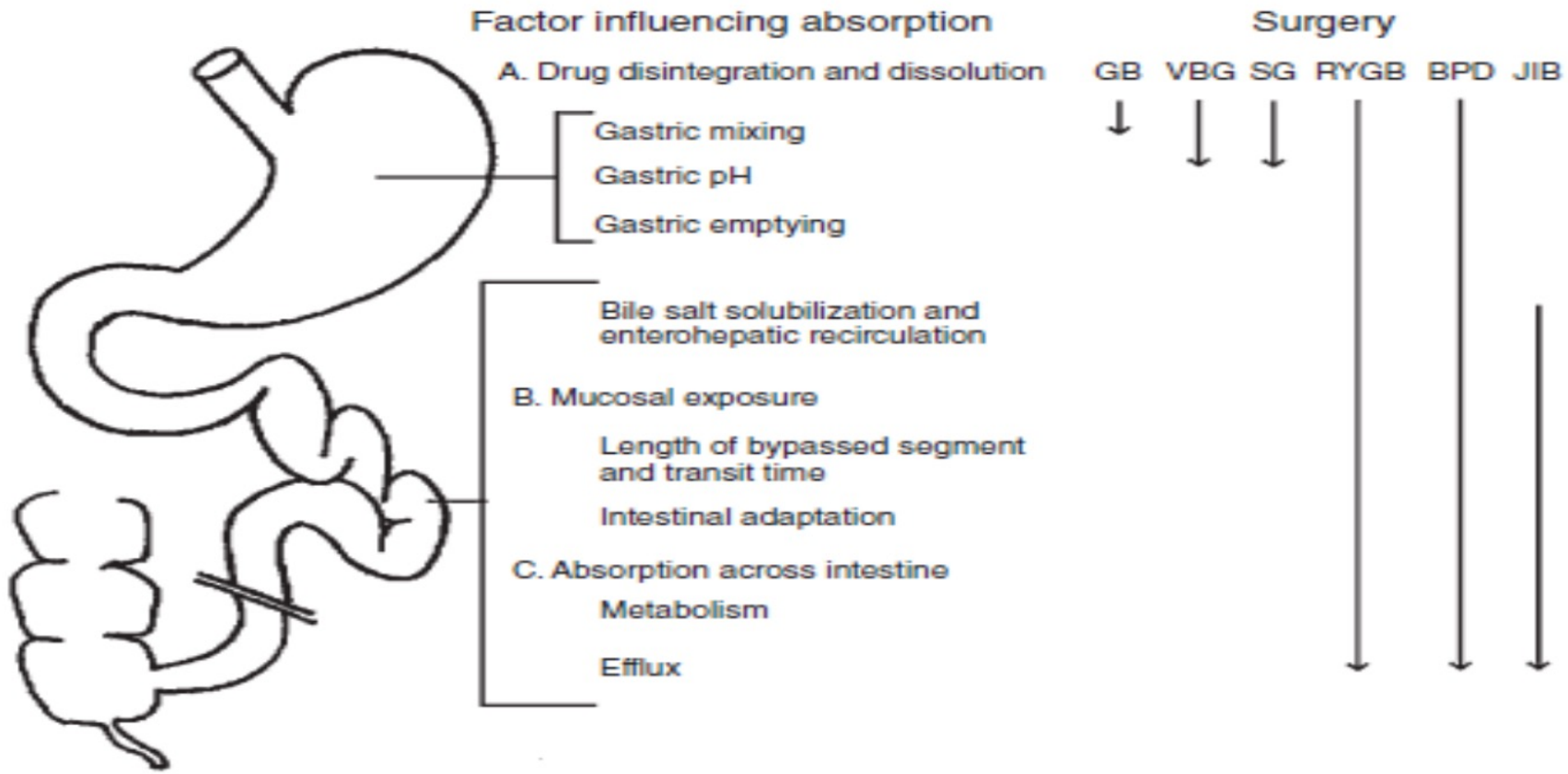
- Dialysis
- Immunosuppression
- Renal failure associated comorbidities
- Risk of Cardiac event, Stroke, Bleeding risks with platelet dysfunction

Dialysis

- Dialysis should be performed day prior to surgery
- Plan for dialysis POD #1
- Transplant Nephrology consult

Immunosuppression

Theoretical effect of various bariatric procedures on factors influencing drug absorption



Post operative Diet in Hospital

- All medications must be given in crushed or liquid form
- Clear Liquid Diet does NOT include anything carbonated
- If patient is on Dialysis, daily fluid intake should NOT exceed 1.5 Liters

Progression	Diet Order	Amount/Time
POD #0 (Day of surgery until 8:00 the next morning)	NPO	N/A
POD #1 30 ml every hour x 3 hours	Sips of Clear Liquids-No carbonated drinks	30 ml @ 8:00 am 30 ml @ 9:00 am 30 ml @ 10:00 am
POD #1 250 ml every 3 hours x 2	Clear liquid diet	250 ml @ 11:00 am 250 ml @ 2:00 pm
POD #1 300-500 ml of fluids for dinner	Clear liquid diet	300-500 ml @ 5:00 pm (dinner) and at each meal up to discharge

Post operative Diet Advancement

- In hospital
  - Clear liquids
  - Discharge home POD #1 when able to tolerate 300-500 mls clear liquids

- At home
  - Resume whey protein powder supplement
  - Clear liquids x 5 days
  - RD calls patient after 5 days and advances to full liquid diet

Post operative Diet

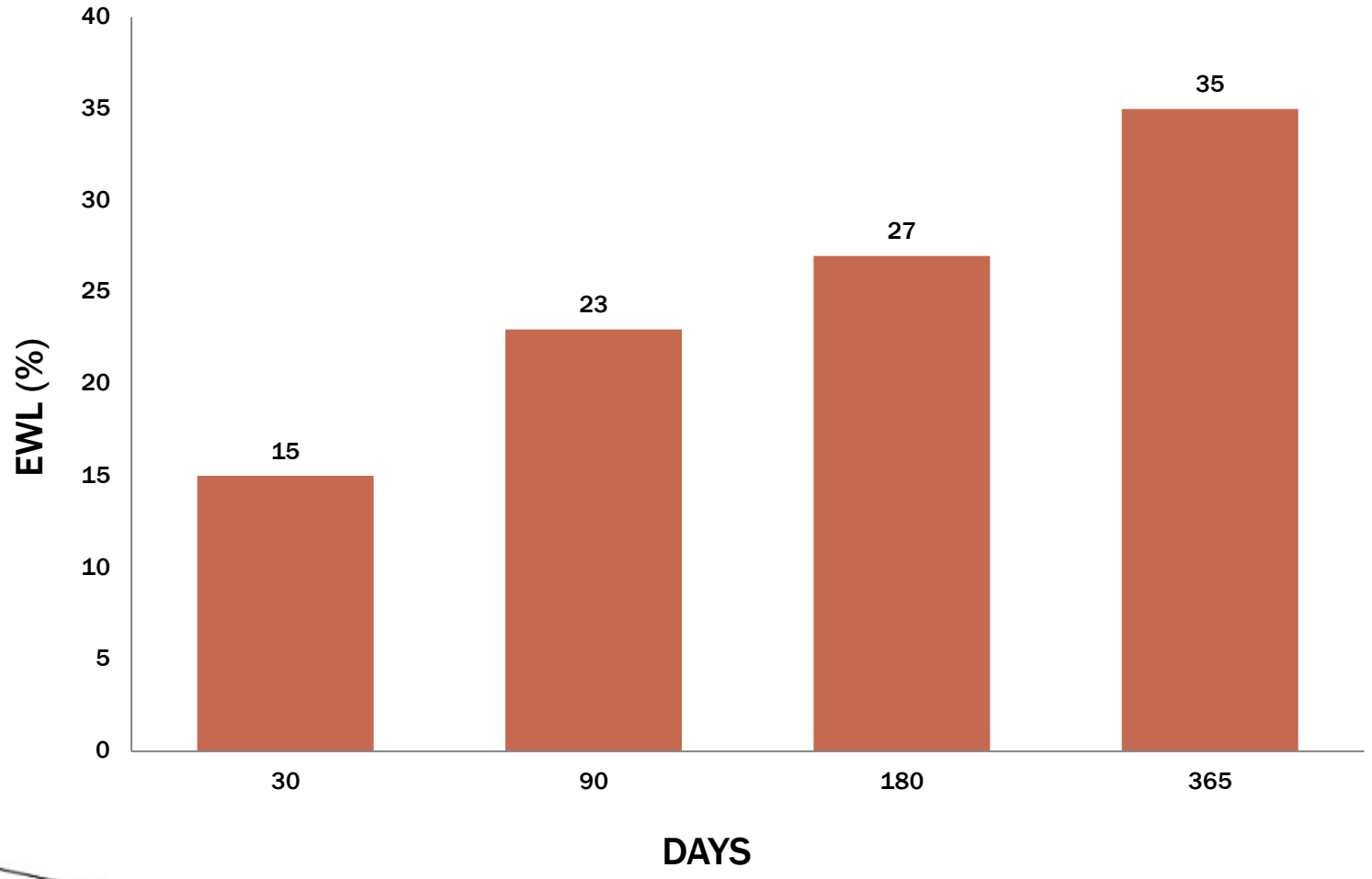
- 2 weeks post-op patient returns to clinic
  - Diet advanced to Pureed foods by RD
- 2-3 weeks later patient returns to clinic
  - Diet advanced to Soft foods by RD
- 2 weeks later patient returns to clinic
  - Maintenance diet initiated by RD

Length of time	5 days	1 week	2 weeks	2-3 weeks	2 weeks- Maintenance
Diet	Clear Liquid + Protein supplement	Full Liquid + Protein supplement	Pureed + protein supplement.	Soft foods +Protein supplement	Regular diet
Sample Foods	Chicken Broth Sugar Free Jello Sugar Free Popsicles, Crystal light	Creamed soups Non fat milk or soy milk Lite blended yogurt Sugar free pudding	Pureed chicken, turkey, or fish Peeled and pureed fruits and vegetables Pudding Oatmeal Yogurt	Moist/very tender meats Soft cooked vegetables Soft noodles Canned fruits	Balanced diet of fluid, fat, carbohydrates and protein. Rich in fruits, vegetables, whole grains, low fat dairy and lean protein
Foods to avoid	Milk products	Thick or lumpy liquids (cream soups that are not pureed)	Tough meats Fibrous fruits or vegetables.	Tough meats Fibrous fruits or vegetables	Tough meats Fibrous fruits and vegetables Fried foods Carbonation Alcohol

General Dietary Guidelines

- Eat 3 (to 6) small meals per pay
- Include lean protein sources, low-fat dairy, at least 5 servings of fruits and veggies
- Take small bites and chew thoroughly
- Avoid drinking beverages for 30 minutes after eating
- Consume 1.5 liters/day of non-caloric, non carbonate fluids
- Avoid concentrated sweets and added sugars
- Avoid Alcohol
- Focus on texture – liquids are less satiating than solids
- No need for Vitamin supplementation

Estimated Weight Loss after LSG



https://www.obesitycoverage.com/gastric-sleeve-reference-manual

Advantages of Gastric Sleeve

- Unlike the gastric band, no abdominal port is required for adjustment, since the stomach is permanently changed
- The part of the stomach where the hunger hormone is made is removed in the procedure, which also helps reduce that hungry feeling
- The procedure can be revised, either by performing a second gastric sleeve, adding a gastric bypass or placing a band at the top of the stomach
- Gastric sleeve patients do not experience dumping syndrome that can happen with a gastric bypass when food is passed too quickly form the stomach into the intestines. Dumping syndrome can cause nausea, vomiting, cramping, diarrhea, dizziness or other stomach-flu-like symptoms

Considerations for Gastric Sleeve

- The gastric sleeve procedure is not adjustable or reversible
- Like any surgery, the potential for complications exists, including a leak in the staple line, which requires immediate care and additional surgery
- After the procedure, it is very important that gastric sleeve patients follow their prescribed post-surgery instructions and make it to their routine office visits
- Patients will need to take a multivitamin and B12 supplement after having gastric sleeve

Lap Sleeve Gastrectomy: UC experience

- 142 ESKD patients underwent Sleeve Gastrectomy (SG) from 2011-2016
- These patients are followed-up and re-evaluated on a regular basis to determine their candidacy for transplantation
- 20 of these patients underwent KT
- This was the largest case series at that time

American Journal of Transplantation
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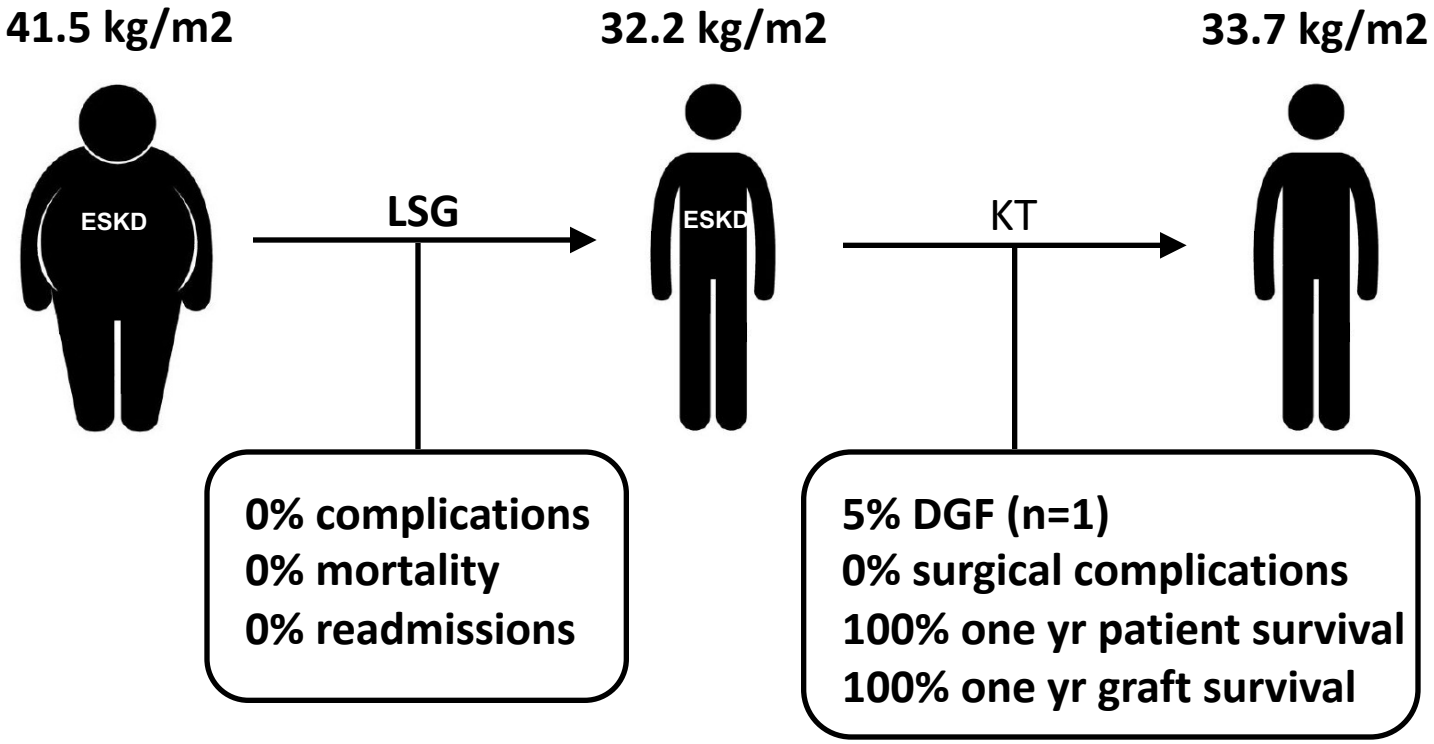
Original Article | Free Access

Addressing Morbid Obesity as a Barrier to Renal Transplantation With Laparoscopic Sleeve Gastrectomy

C. M. Freeman, E. S. Woodle, J. Shi, J. W. Alexander, P. L. Leggett, S. A. Shah, F. Paterno, M. C. Cuffy, A. Govil, G. Mogilishetty, R. R. Alloway, D. Hanseman, M. Cardi, T. S. Diwan

First published:23 February 2015 | https://doi.org/10.1111/ajt.13116 | Citations: 40

TRIMS: The UC Experience 2015



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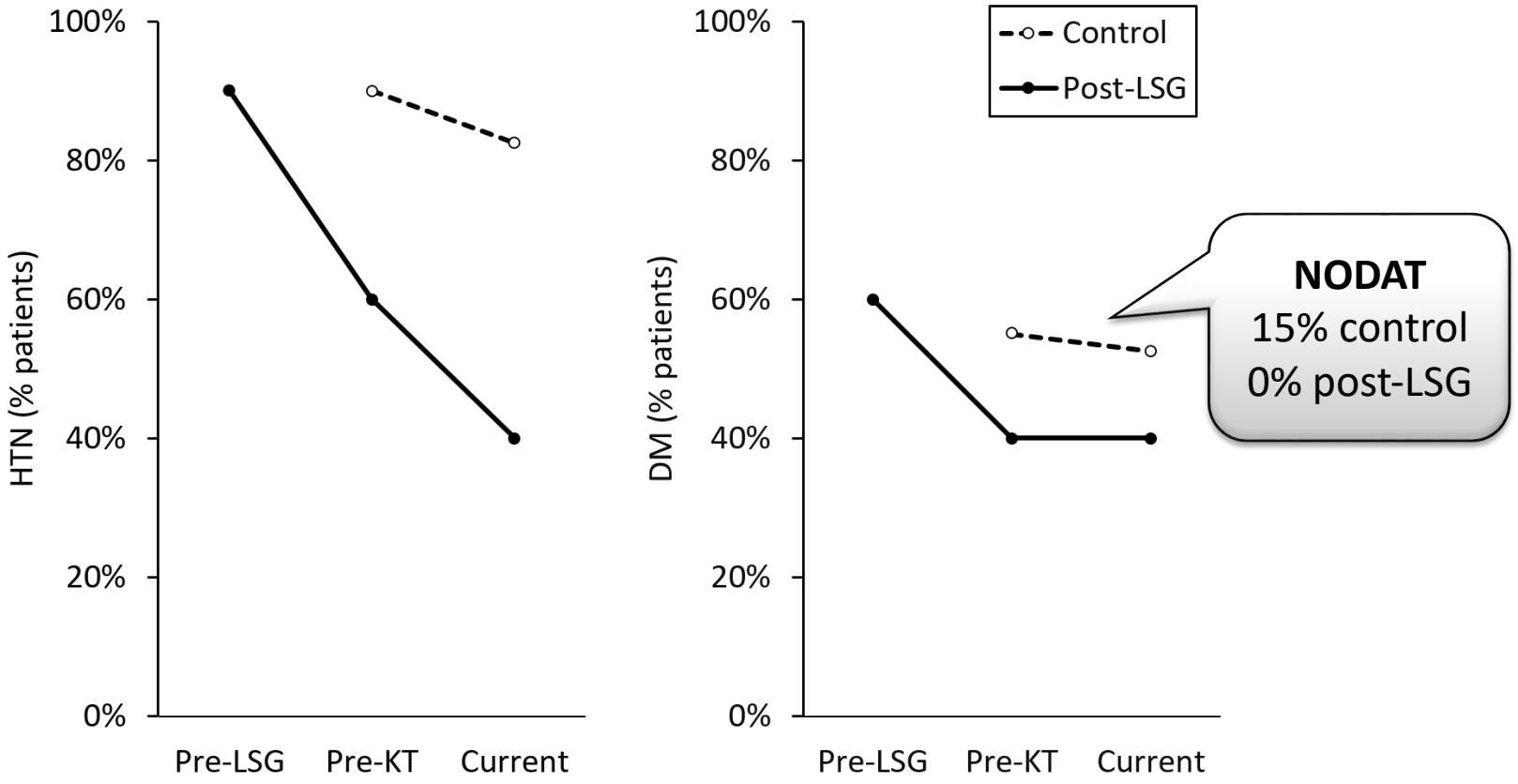
Comparing obesity-related comorbidities



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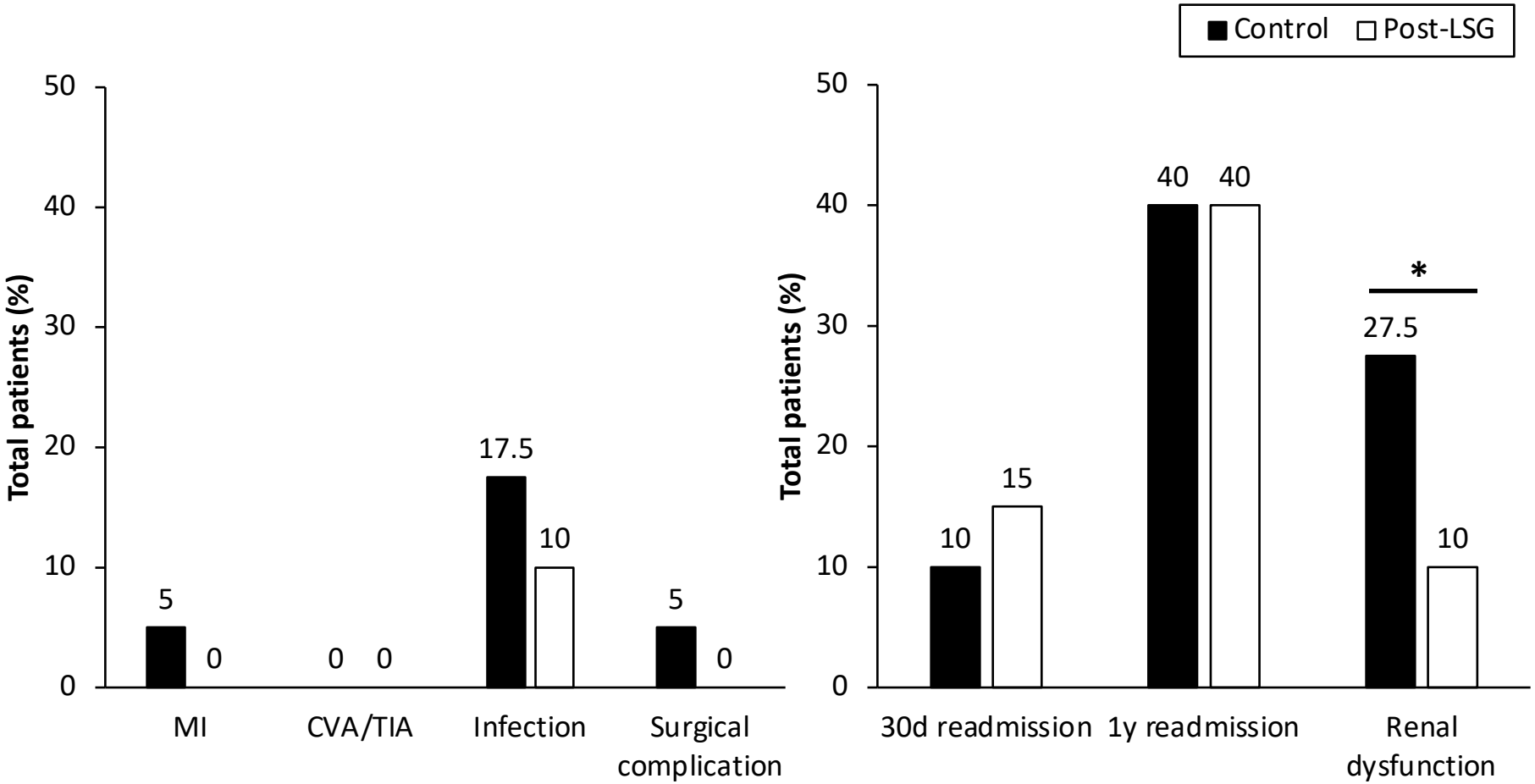
Comparing short-term outcomes



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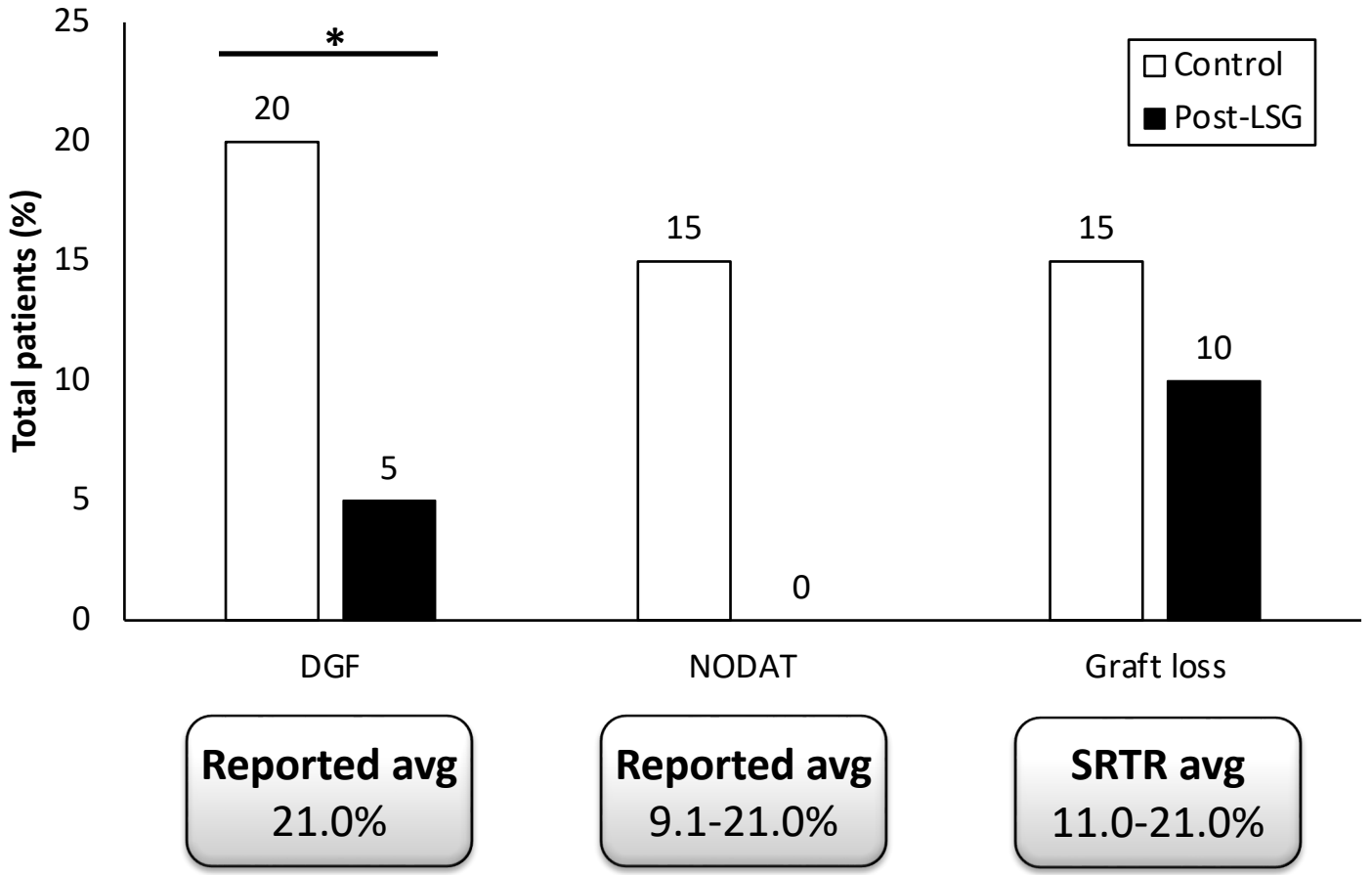
Comparing long-term outcomes



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TRIMS: Conclusions 2015

- SG is safe and effective among ESKD patients
- SG improves transplant candidacy among morbidly obese ESKD patients
  - 20 of 142 patients transplanted during study period
- Short- and long-term posttransplant outcomes are similar or better among post-SG patients compared with patients of a similar BMI and patient profile
  - Readmission due to kidney dysfunction
  - Delayed graft function

AJT Feb.2020 cover

Impact Factor: 7.163

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ORIGINAL ARTICLE

Long-term outcomes in patients with obesity and renal disease after sleeve gastrectomy

Al-Faraaz Kassam, Ahmad Mirza, Young Kim, Dennis Hanseman, E. Steve Woodle, Ralph C. Quillin III, Bobby L. Johnson, Amit Govil, Michael Cardi, Daniel P. Schauer, Eric P. Smith, Tayyab S. Diwan

First published: 12 October 2019 | https://doi.org/10.1111/ajt.15650 | Citations: 1

“Largest series to date of laparoscopic sleeve gastrectomy in morbidly obese chronic kidney disease and end-stage kidney disease patients who were simultaneously being evaluated for kidney transplant.”

American Journal of Transplantation
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ORIGINAL ARTICLE

Long-term outcomes in patients with obesity and renal disease after sleeve gastrectomy

- **Prospective**ly collected data on patients with ESKD and chronic kidney disease (CKD) undergoing Sleeve Gastrectomy (SG) from **2011 to 2018**
- **198 patients with ESKD and 45 patients with CKD** (stages 1-4) who met National Institutes of Health guidelines for bariatric surgery and underwent SG
- **72%** achieved a BMI of **≤ 40 kg/m^2**
- **48%** achieved a BMI of **≤ 35 kg/m^2**
- The mean % of total weight loss **18.9** ± 10.8%
- The mean %of excess weight loss **38.2** ± 20.3%

American Journal of Transplantation
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ORIGINAL ARTICLE

Long-term outcomes in patients with obesity and renal disease after sleeve gastrectomy

- SG **reduced hypertension** (85.8% vs **52.1%**)
- SG **decreased antihypertensive medication use** (1.6 vs **1.0**) (*P* < .01 each)
- SG **reduced incidence of diabetes** (59.6% vs **32.5%**, *P* < .01)
- 71 patients with ESKD achieved a body mass index of ≤ 40 kg/m^2 (**45 received a kidney transplant, 10 remain on the waitlist**)
- **Mortality rate** after SG was **1.8 per 100 patient-years**, compared with 7.3 for non-SG
- Patients with stage 3a or 3b CKD exhibited **improved glomerular filtration rate** (43.5 vs **58.4** mL/min, *P* = .01)

UC College of Medicine

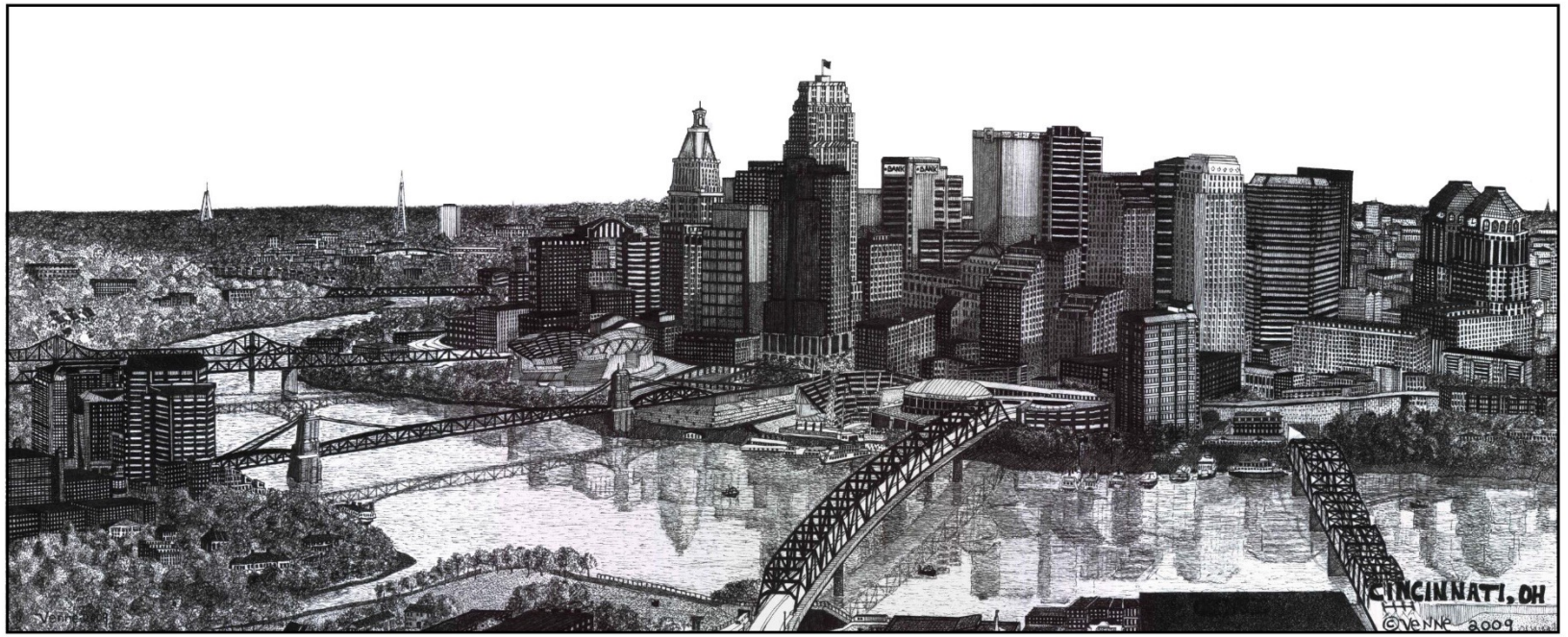
Conclusions

- Morbid Obesity is a significant barrier to transplantation and adds to overall increased morbidity and mortality
- Sleeve Gastrectomy performed in a multi disciplinary set up is a safe and effective procedure for weight loss
- Sleeve Gastrectomy safely
  - improves transplant candidacy
  - provides significant, sustainable effects on weight loss,
  - reduces medical comorbidities
  - possibly improves kidney function in stage 3 patients

1 Million Transplants in U.S. in last 68 years

1954-2022

Getting to the Next Million Transplants…



Cincinnati, Ohio

UC Health Kidney Transplant Team

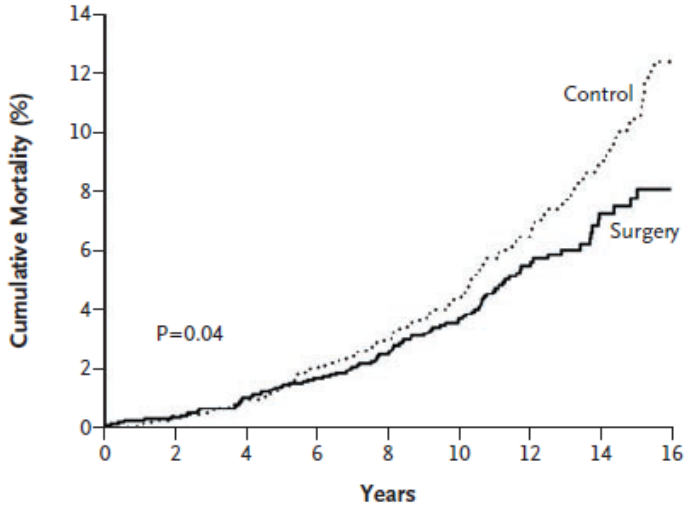
Outcomes

Metabolic Surgery Reduces Mortality

- Swedish Obesity Study
- >4000 pts randomized to surgery or control
- Mean follow up 10.9 yrs (99.9% follow up)
- Most frequent causes of death – cancer and myocardial infarction

The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 AUGUST 23, 2007 VOL. 357 NO. 8

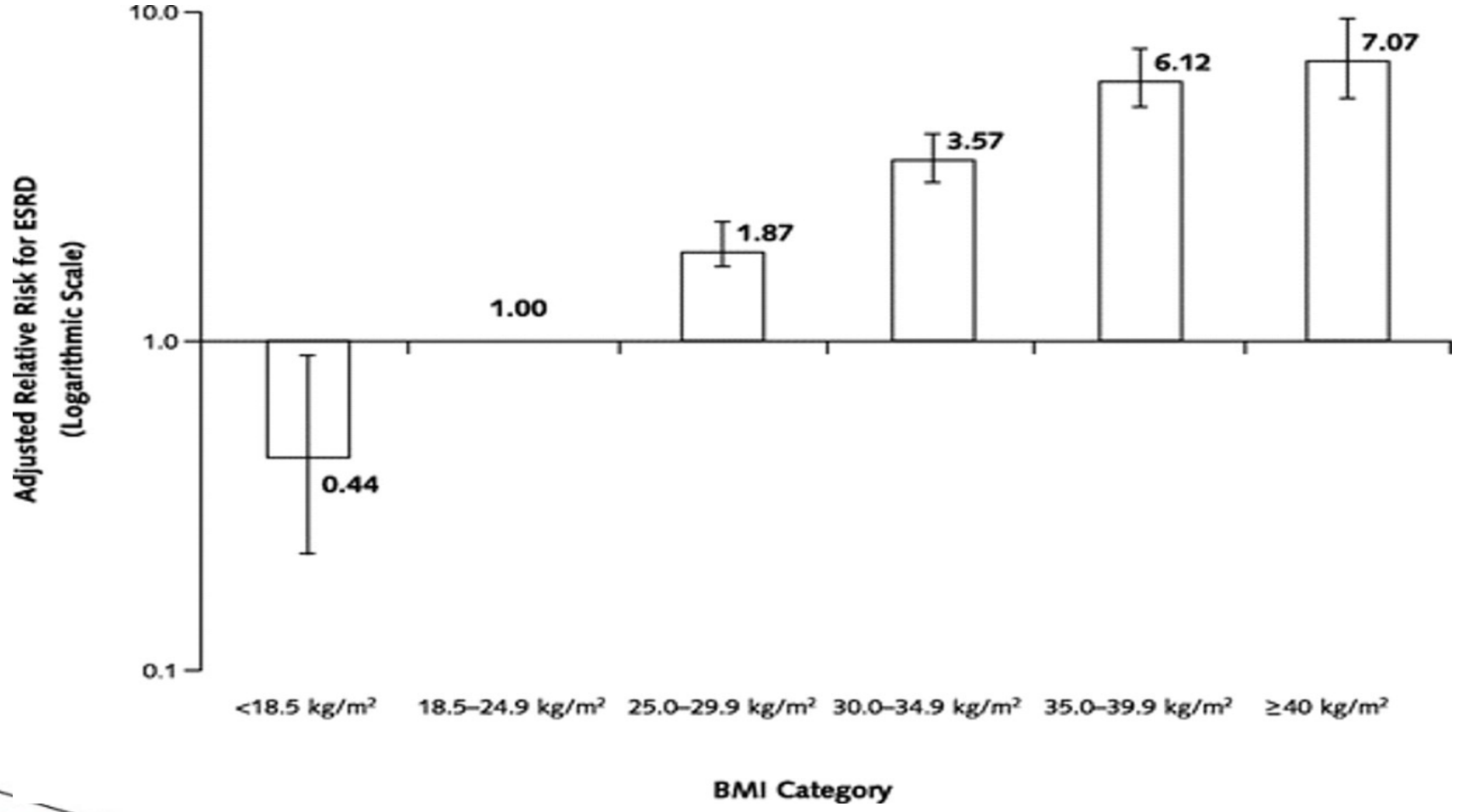
Effects of Bariatric Surgery on Mortality in Swedish Obese Subjects



No. at Risk									
Surgery	2010	2001	1987	1821	1590	1260	760	422	169
Control	2037	2027	2016	1842	1455	1174	749	422	156

Outcomes

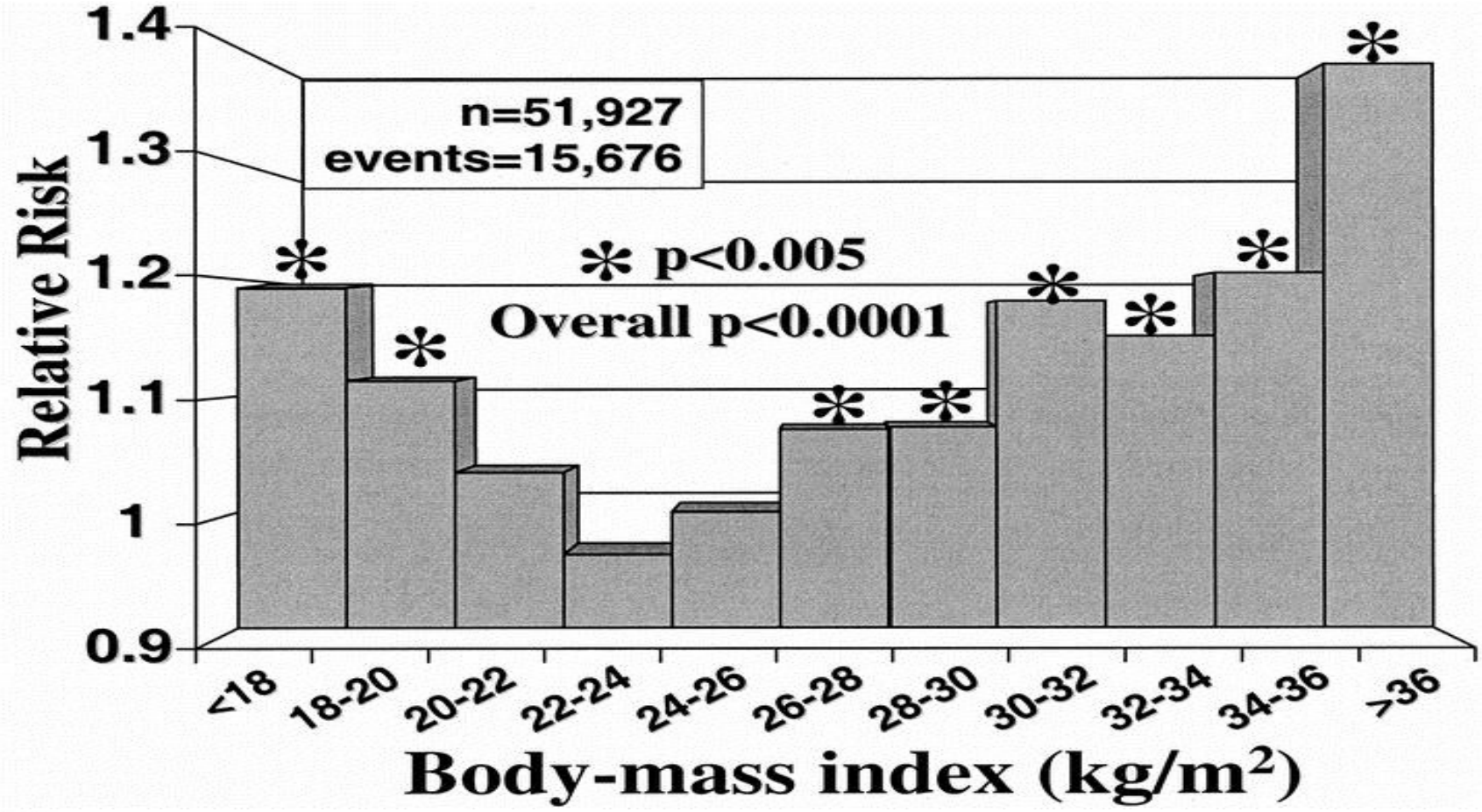
BMI and Risk for ESRD



Hsu, C et. al. Ann Intern Med 2006;144:21-28

Outcomes

Relative Risk of Renal Allograft Loss



51, 927 primary adult transplants in USRDS

Meier-Kriesche, Transplantation, Vol 73(1) 2002