Obesity and Cancer Survival

Corrigan McBride, MD
Professor of Surgery
Director of Bariatric Surgery
Chief of General Surgery, Minimally Invasive and Bariatric Surgery, UNMC

University of Nebraska Medical Center

Nebraska Medicine

Disclosure

Food and Beverage-

- Medtronic
- Davol
- Bard
- Intuitive

Travel for non-CME events- Medtronic

Objectives

Impact of Obesity on Cancer Incidence

Impact on Obesity on Cancer Diagnosis and Therapies

Impact of Obesity Therapies on Cancer Survivorship.

What about the Bariatric Surgery and Medicine such as the GLP-1?

Impact of Obesity on Mortality and Cancer Incidence

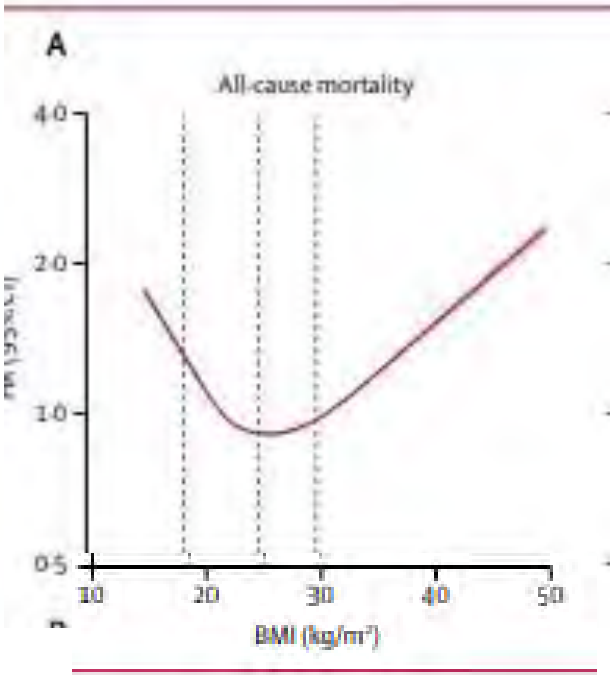
University of Nebraska Medical Center

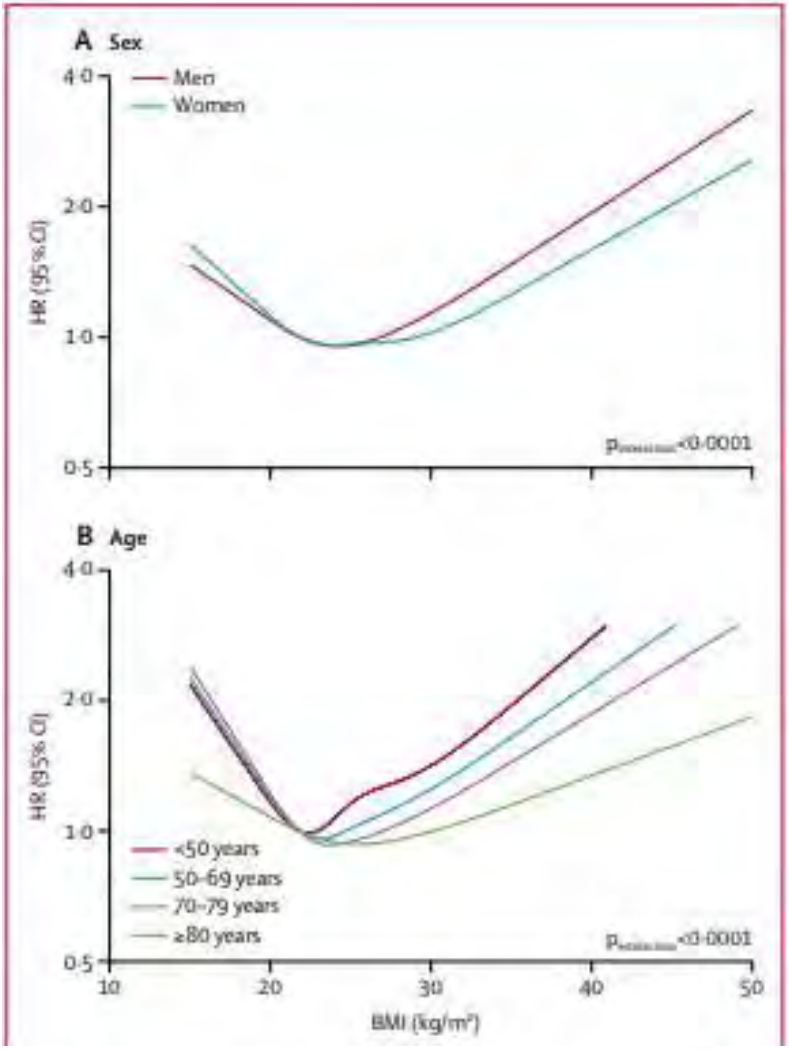
Nebraska Medicine

Association of BMI with overall and cause-specific mortality: a population-based cohort study of 3·6 million adults in the UK

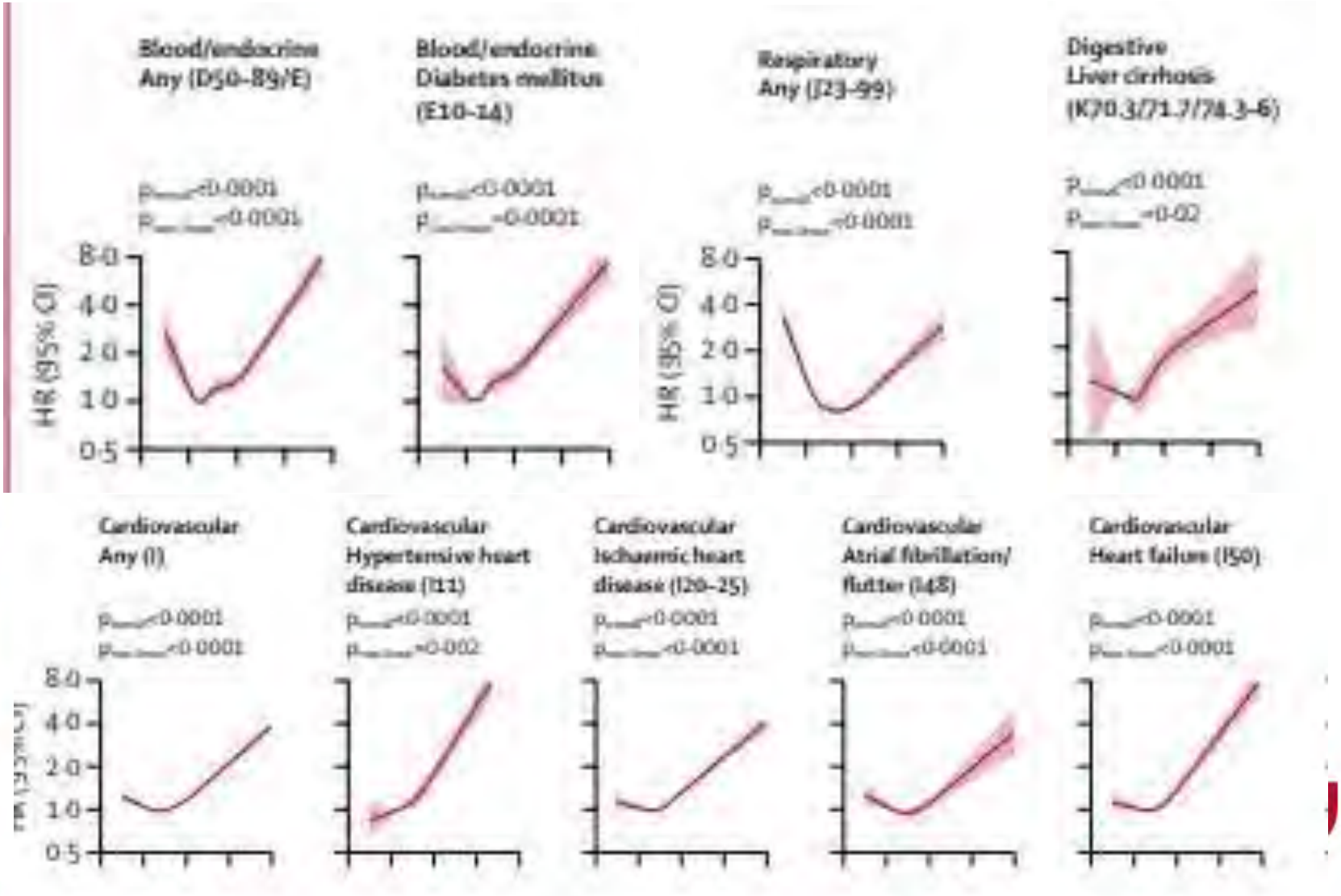
Krishnan Bhaskaran, Isabel dos-Santos-Silva, David A Leon, Ian J Douglas, Liam Smeeth

Obesity is linked to increased mortality



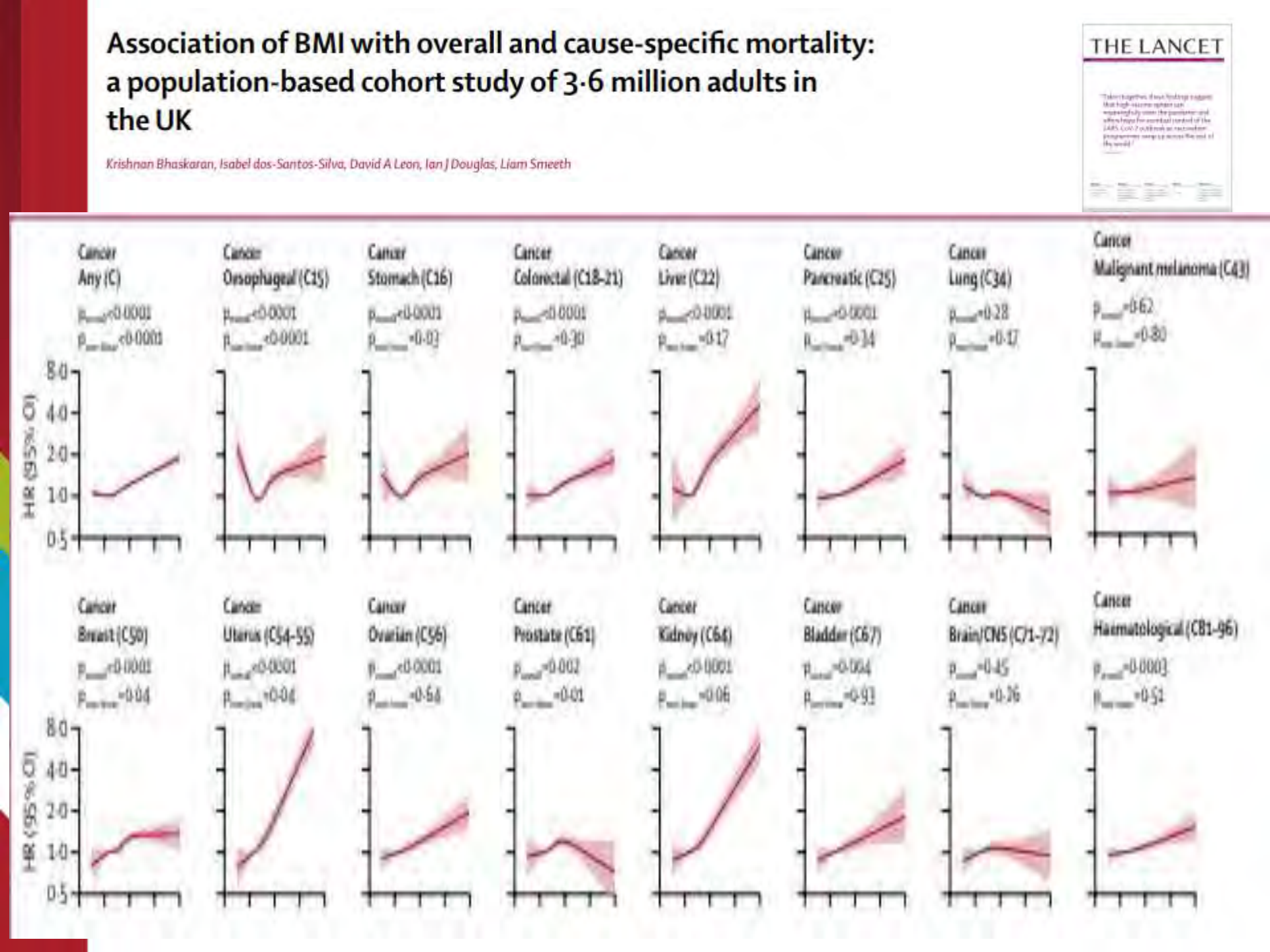


Non-Cancer diagnosis



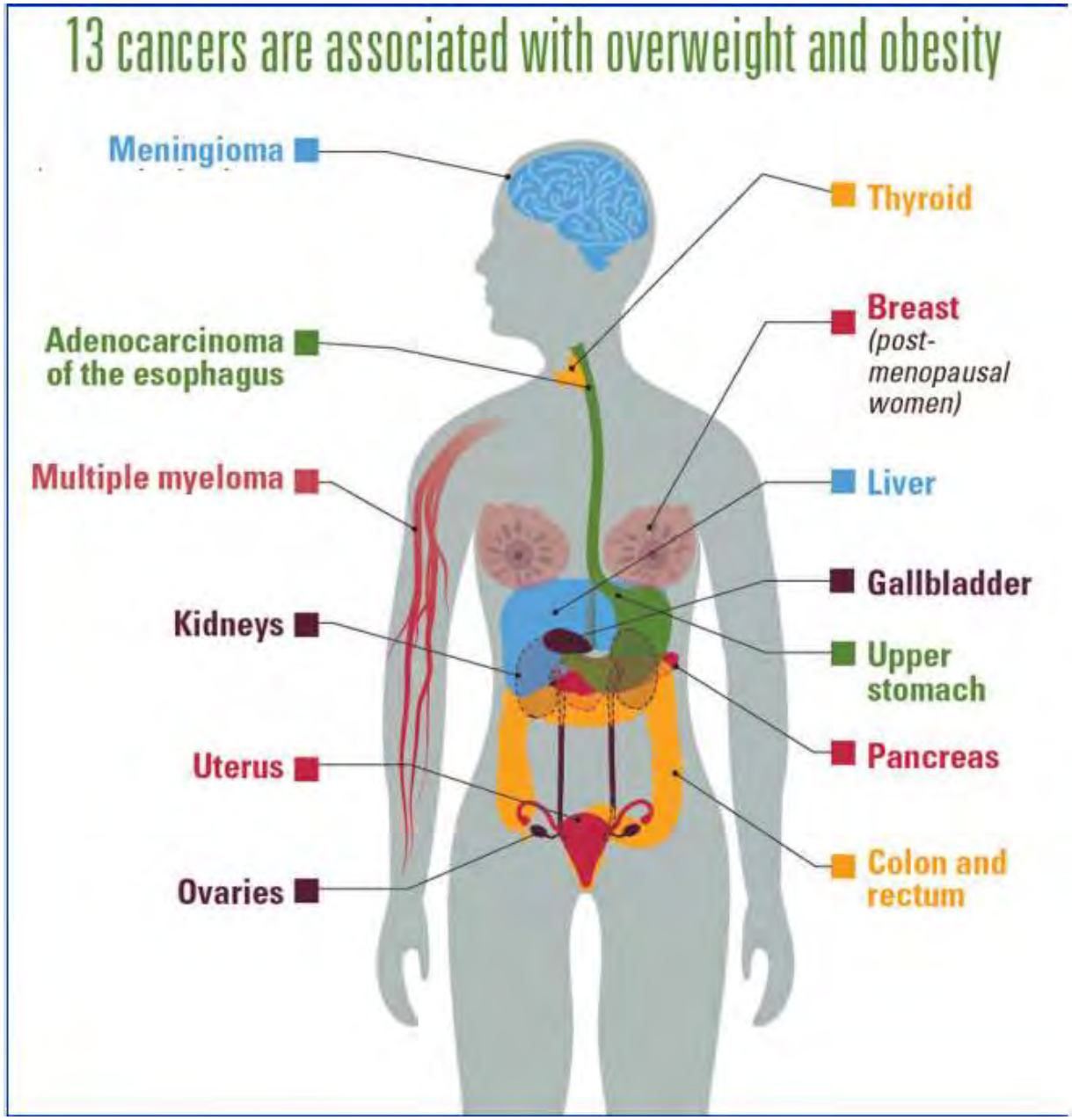
Association of BMI with overall and cause-specific mortality: a population-based cohort study of 3·6 million adults in the UK

Krishnan Bhaskaran, Isabel dos-Santos-Silva, David A Leon, Ian J Douglas, Liam Smeeth



Effect of Obesity on Life Expectancy at Age 40

	Men		Women	
BMI (kg/m^2)	Life Expectancy at age 40	Reduction in life expectancy	Life Expectancy at age 40	Reduction in life expectancy
< 18.5	77.9	4.3	79.8	4.5
18.5-24.9	82.2	Referent	84.3	Referent
25.0-29.9	81.2	1.0	83.5	0.8
30.0-34.9	78.7	3.4	81.9	2.4
35.0-39.9	76.2	5.9	79.6	4.7
≥ 40.0	73.1	9.1	76.6	7.7


13 cancers are associated with overweight and obesity
Meningioma
Adenocarcinoma of the esophagus
Multiple myeloma
Kidneys
Uterus
Ovaries
Thyroid
Breast (post-menopausal women)
Liver
Gallbladder
Upper stomach
Pancreas
Colon and rectum

Summary risk estimate per 5 kg/m^2

Location	Men	Women	Strength of Evidence
Esophageal (adeno)	1.52	1.51	Convincing
Gastric (adeno)	0.97	1.04	Probable
Colorectal (adeno)	1.09-1.24	1.02-1.04	Convincing
Gallbladder	1.09	1.59	Probable
Pancreatic (adeno	1.13	1.10	Convincing
Liver (HCC)	1.19	1.12	Convincing
Renal	1.24	1.34	Convincing
Breast (post menopausal		1.12	Convincing
Endometrial		1.59	Convincing
Ovarian		1.06	Probable
Prostate	1.08		Probable

https://doi.org/10.1016/j.metabol.2018.11.001

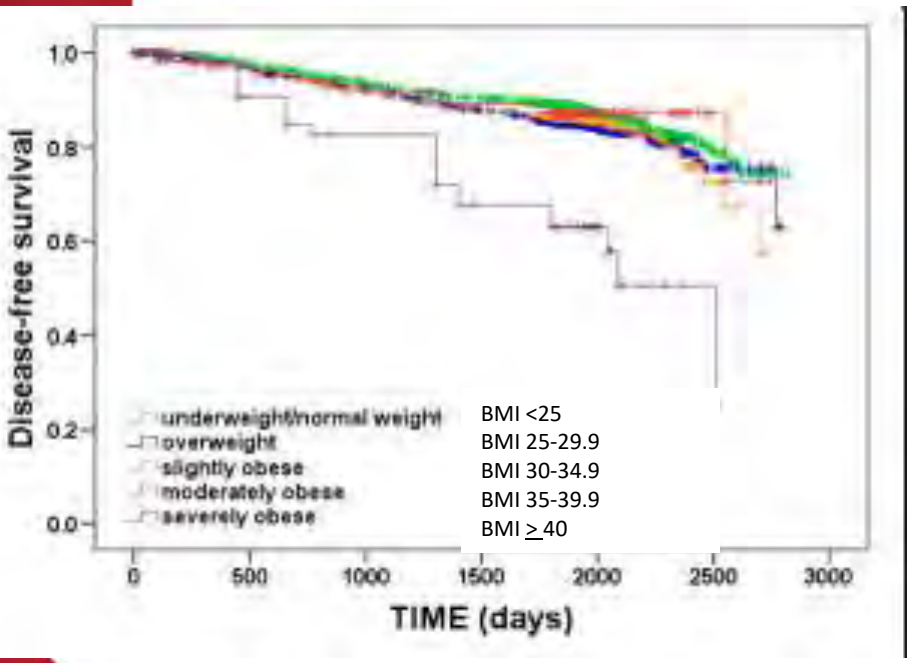
Obesity impacts Therapy

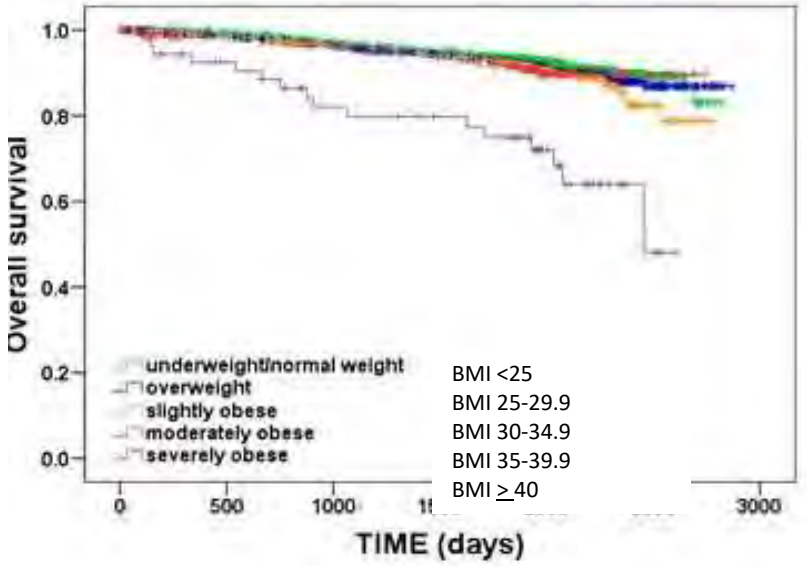
University of Nebraska Medical Center

Nebraska Medicine

The influence of obesity on survival in early, high-risk breast cancer: results from the randomized SUCCESS A trial

Peter Widschwendter[1*†], Thomas WP Friedl[1†], Lukas Schwentner[1], Nikolaus DeGregorio[1], Bernadette Jaeger[1], Amelie Schramm[1], Inga Bekes[1], Miriam Deniz[1], Krisztian Lato[1], Tobias Weissenbacher[2], Bernd Kost[2], Ulrich Andergassen[2], Julia Jueckstock[2], Julia Neugebauer[2], Elisabeth Trapp[2], Peter A. Fasching[3], Matthias W. Beckmann[3], Andreas Schneeweiss[4], Ines Schrader[5], Brigitte Rack[2], Wolfgang Janni[1] and Christoph Scholz[1]





Widschwendter *et al. Breast Cancer Research* (2015) 17:129
DOI 10.1186/s13058-015-0639-3

The Impact of Obesity on Breast Cancer Diagnosis and Treatment

Kyuwan Lee [1] · Laura Kruper [2] · Christina M. Dieli-Conwright [1] · Joanne E. Mortimer [3,4]

1. Challenges of Diagnosis
    1. The incidence of False negative was comparable across BMI
    2. Stigma of Obesity decreases patient willingness to seek health care
2. Surgical Interventions
    1. Trend toward moving to breast conservation therapy
        1. Some studies suggest that the risk of local recurrence is higher in obese patients
        2. Sentinel lymph node identification is lower in women with obesity.
    2. Obesity is a higher risk of surgical complications in mastectomy patients
3. Systemic therapy
    1. Patients with obesity require higher doses of systemic tx to get tumor suppression with some regimens
    2. Studies that show less benefit of endocrine therapy after treatment on patients with obesity.

Current Oncology Reports (2019) 21: 41
https://doi.org/10.1007/s11912-019-0787-1

Weight Stigma

Medical Students and NP students report observing weight shaming and weight bias on their clinical rotations.

While some providers think that this behavior will “motivate” patients to work on their weight and health, the opposite is true.

- Patients who experience health care related weight bias are more likely to exhibit unhealthy eating patters, binge eating, and less likely to engage in physical activity.

Remember Obesity is a Disease

You don’t say a 42-year-old cancer patient, it is a 42-year-old patient with cancer

Table 1. People-First Language is critical to reducing bias and discrimination

Example of People-First Language	Example of Non-People-First Language
A 43-y-old female patient with obesity	A 43-y-old obese female patient
A study related to children with obesity	A study of obese children

Weight Stigma

Table2. Strategies to reduce obesity bias and stigma: compassionate and respec
communication

Encouraged terms	Discouraged Terms
Weight	Morbidly obese
Unhealthy weight	Obese
Overweight	Fat
Preobesity	Heaviness
Body mass index	Large size
Excessive energy stores	Chubby
Affected by obesity	Plump
Eating habits/nutrition	Big size
Physical activity	Diet
Healthy habits	Exercise

Class I obesity
Class II obesity
Class III obesity

Weight bias and health care utilization: a scoping review

Angela S. Alberga[1], Iyoma Y. Edache[1], Mary Forhan[2] and Shelly Russell-Mayhew[3]

1. Contemptuous treatment- verbal insults, inappropriate humor, treated less respectfully

2. Attribution of all health issues to excess weight

3. Health provider making assumptions about weight gain

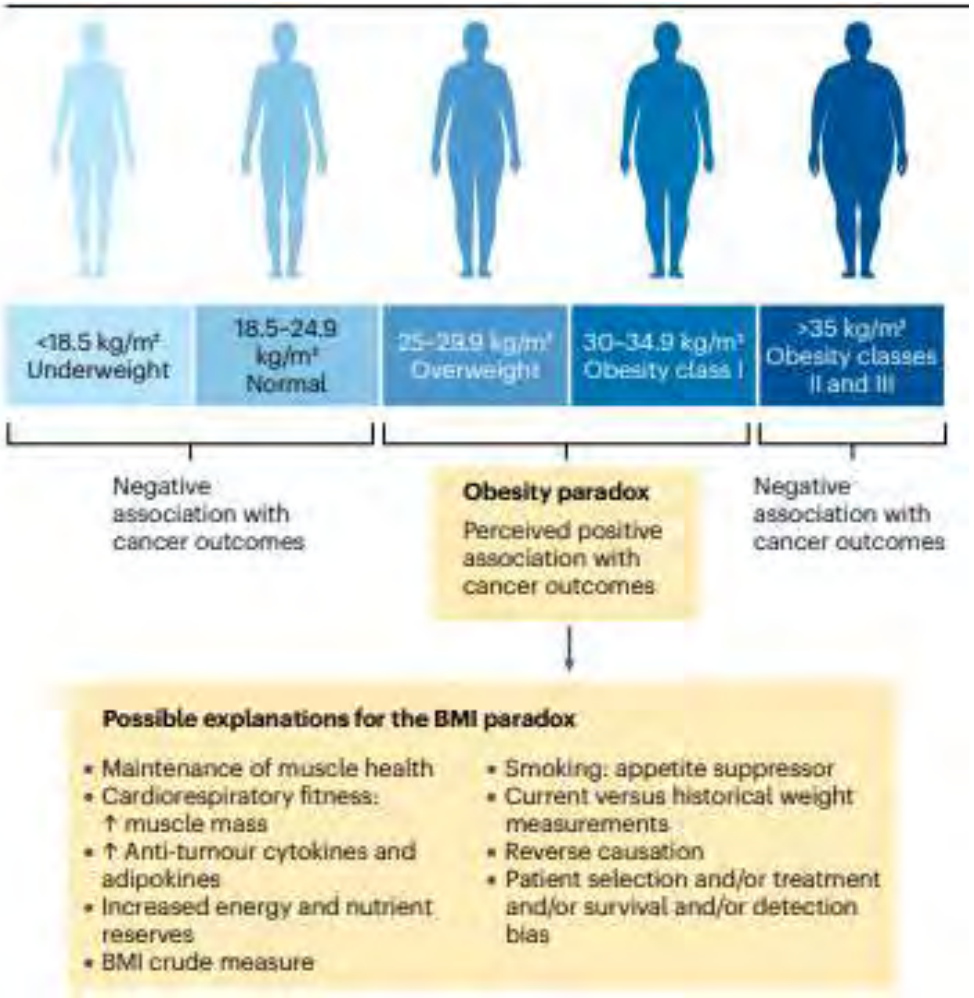
4. Barriers to health care utilization
    1. 7 studies showed avoidance, delay or cancellation of health care services because of
        1. Not wanting to weight
        2. Not wanting to get undressed
        3. Inadequate seating, tables, gowns, BP cuffs, etc

5. Wanting to be seen as a whole person is interpreted as “doctor shopping”

https://doi.org/10.1017/S1463423619000227 Published online by Cambridge University Press

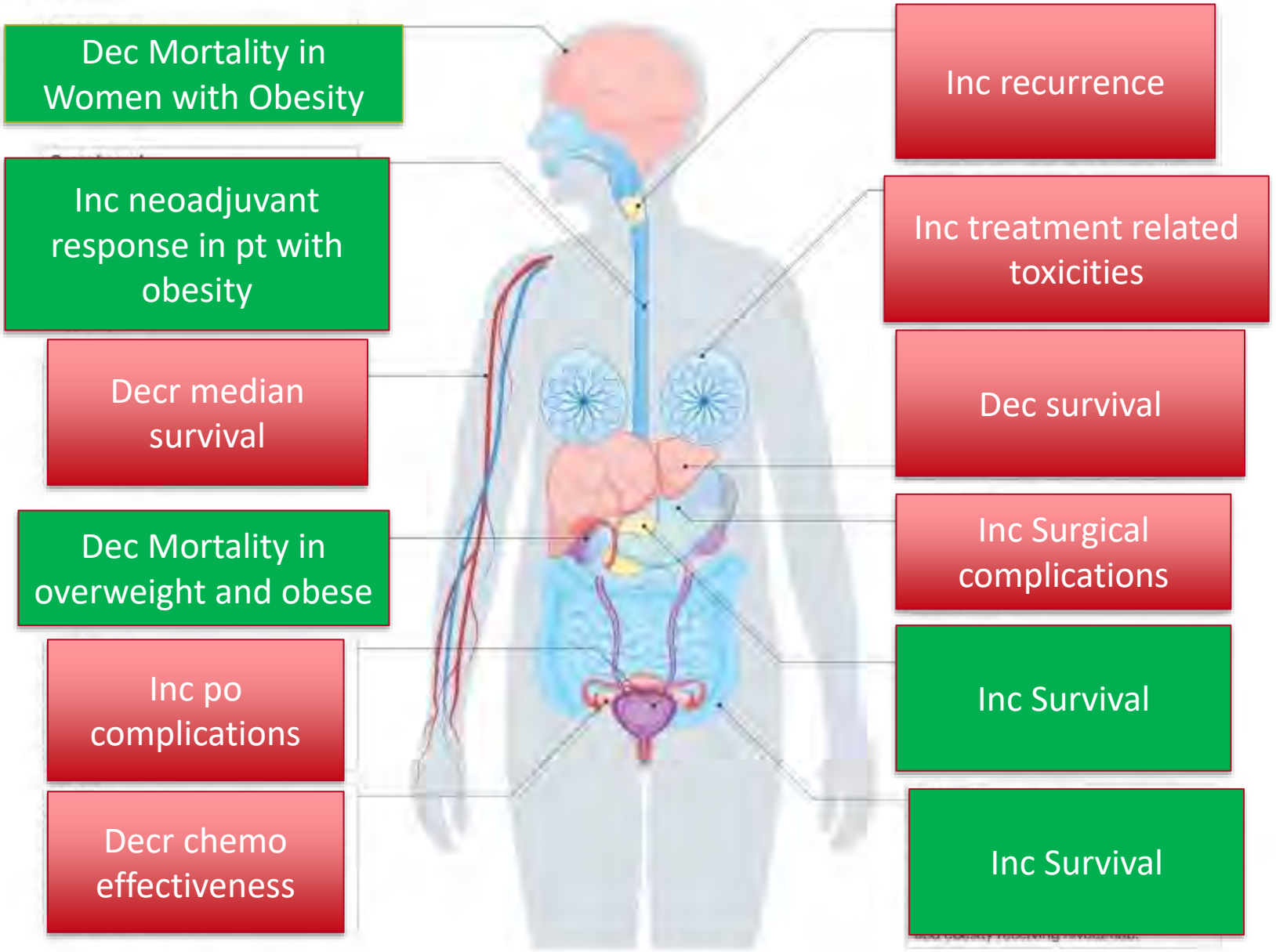
The multifactorial effect of obesity on the effectiveness and outcomes of cancer therapies

Joanne Lysaght [1] & Melissa J. Conroy [2]



https://doi.org/10.1038/s41574-024-01032-5

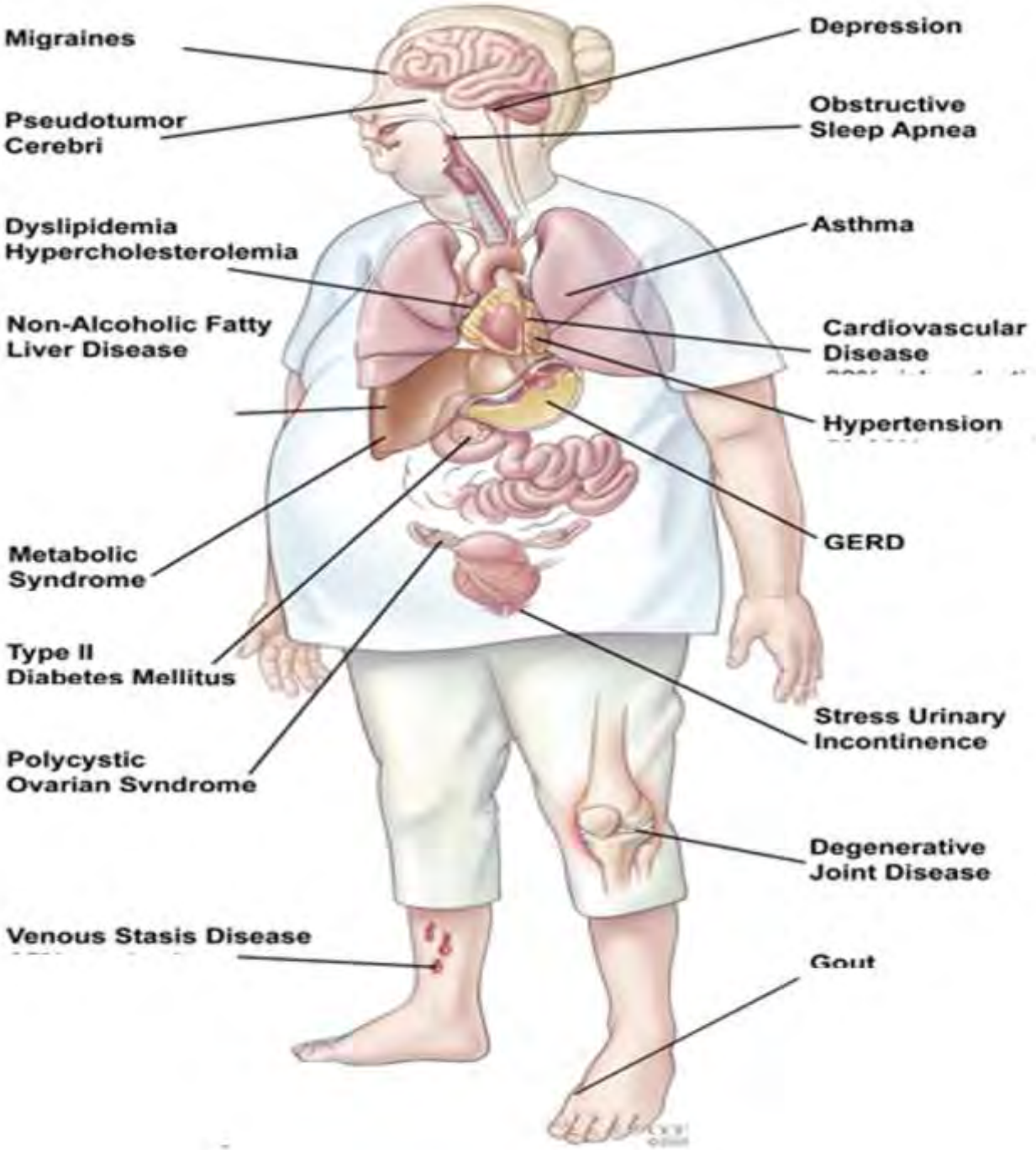
Fig. 1: Obesity-associated cancers, relative risk, treatment efficacy, toxicities and outcomes.



Obesity impacts Co-morbidities

University of Nebraska Medical Center

Nebraska Medicine


Migraines
Depression
Pseudotumor Cerebri
Obstructive Sleep Apnea
Dyslipidemia Hypercholesterolemia
Asthma
Non-Alcoholic Fatty Liver Disease
Cardiovascular Disease
Hypertension
GERD
Metabolic Syndrome
Type II Diabetes Mellitus
Stress Urinary Incontinence
Polycystic Ovarian Syndrome
Degenerative Joint Disease
Venous Stasis Disease
Gout

Cardiovascular disease is the leading cause of death among endometrial cancer patients

Kristy K. Ward *, Nina R. Shah, Cheryl C. Saenz, Michael T. McHale, Edwin A. Alvarez, Steven C. Plaxe

NCI Surveillance, Epidemiology and End Results(SEER)

9 registries

Patients from 1973-1988 (so would have 20-year mortality data)

44,145 patients with endometrial cancer

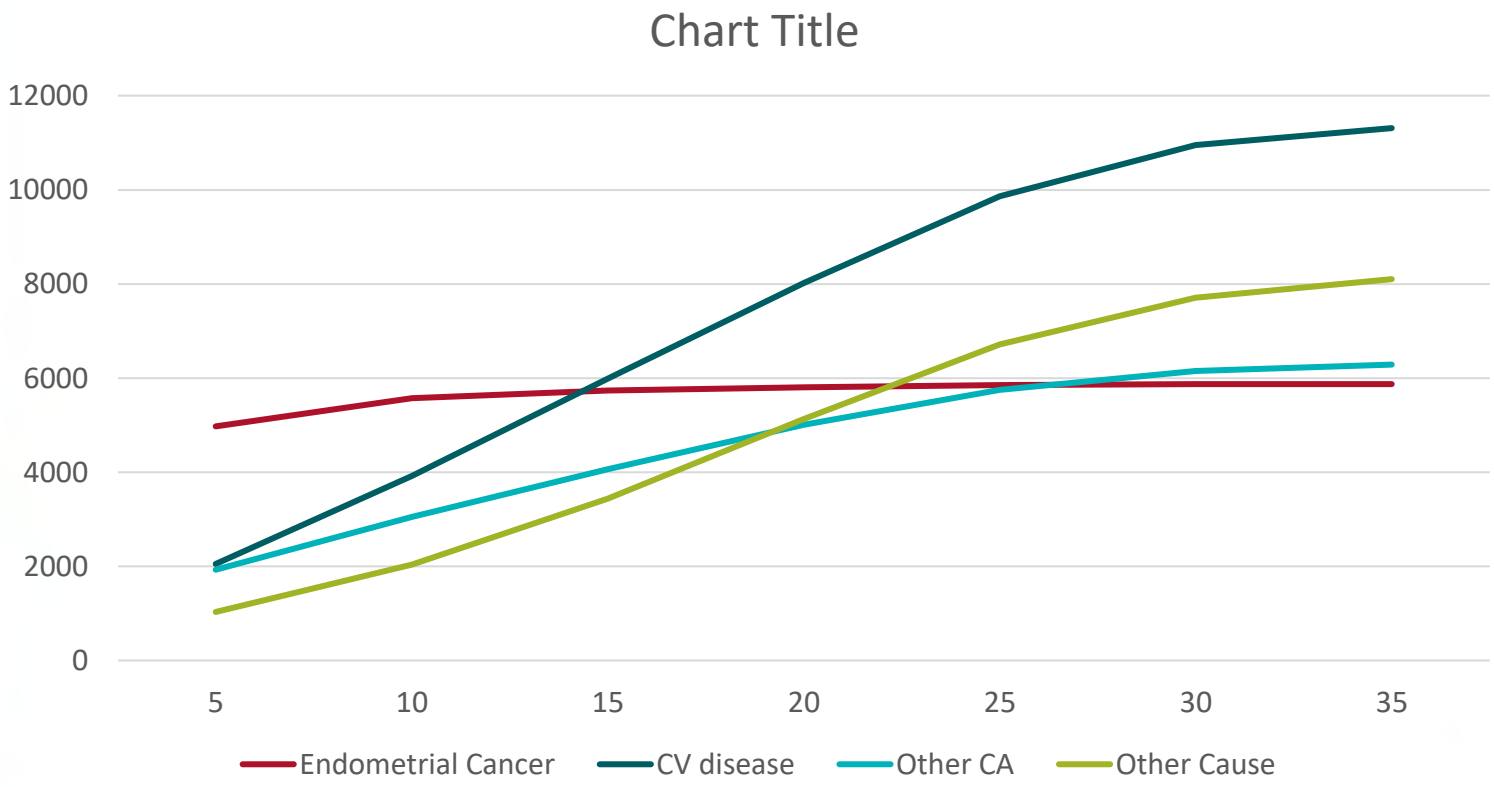
By 2008, 75.3% had died.

96% of patients had known Cause of Death (COD)

Gynecologic Oncology 126 (2012) 176–179

Cardiovascular disease is the leading cause of death among endometrial cancer patients

Kristy K. Ward *, Nina R. Shah, Cheryl C. Saenz, Michael T. McHale, Edwin A. Alvarez, Steven C. Plaxe



Weight Management is an important part of Post Cancer Survivorship

Bariatric Surgery

University of Nebraska Medical Center

Nebraska Medicine

Lap Sleeve Gastrectomy

Remove ~80% of the stomach

Restricts the quantity of food

Removes the ghrelin producing cells, so not hungry

No foreign body

Laparoscopic, overnight stay

Irreversible

Potential for vitamin deficiency, B vit, Fe

Risks of Leak, DVT/PE, portal vein thrombosis

Weight loss ~20-25% of total body weight

Lap Gastric Bypass

Gold Standard Operation

Restricts the amount of food

Because no food contacts the antrum, there is a decrease in ghrelin (less hunger) and undigested food hit small intestine faster there is an increase in leptin (early satiety)

Risks- Leak, DVT/PE,

Long term vitamin def- Fe, B12, Ca, Vit D.

Ulcers-smoking, NSAID, steroids,

Internal hernia

Weight loss ~25-30% of total body weight

Lap Duodenal Switch, SADI-S

Decrease risks of internal hernia,ulcers, re weight gain

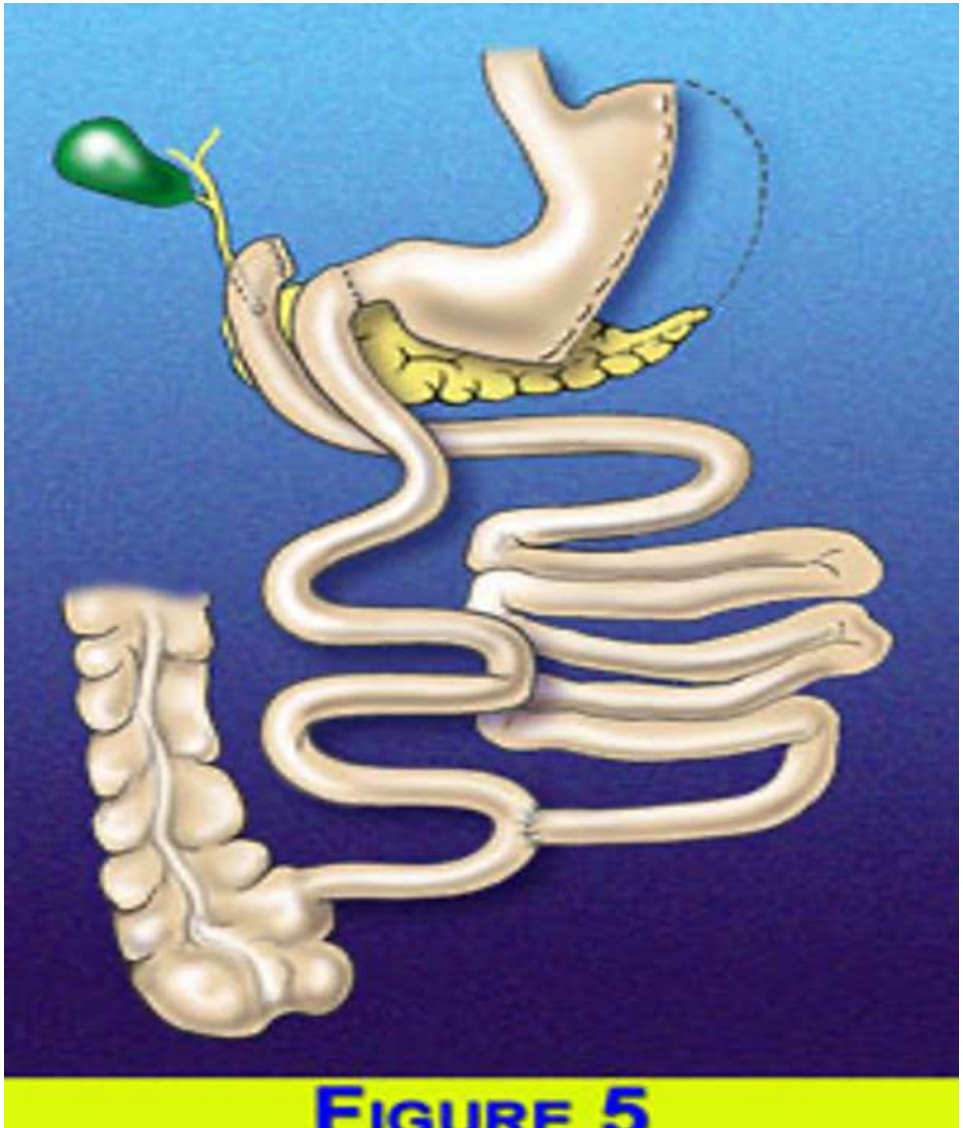
Can take NSAIDS, steroids with much lower risk of ulcers, no dumping with sugar (pylorus in place)

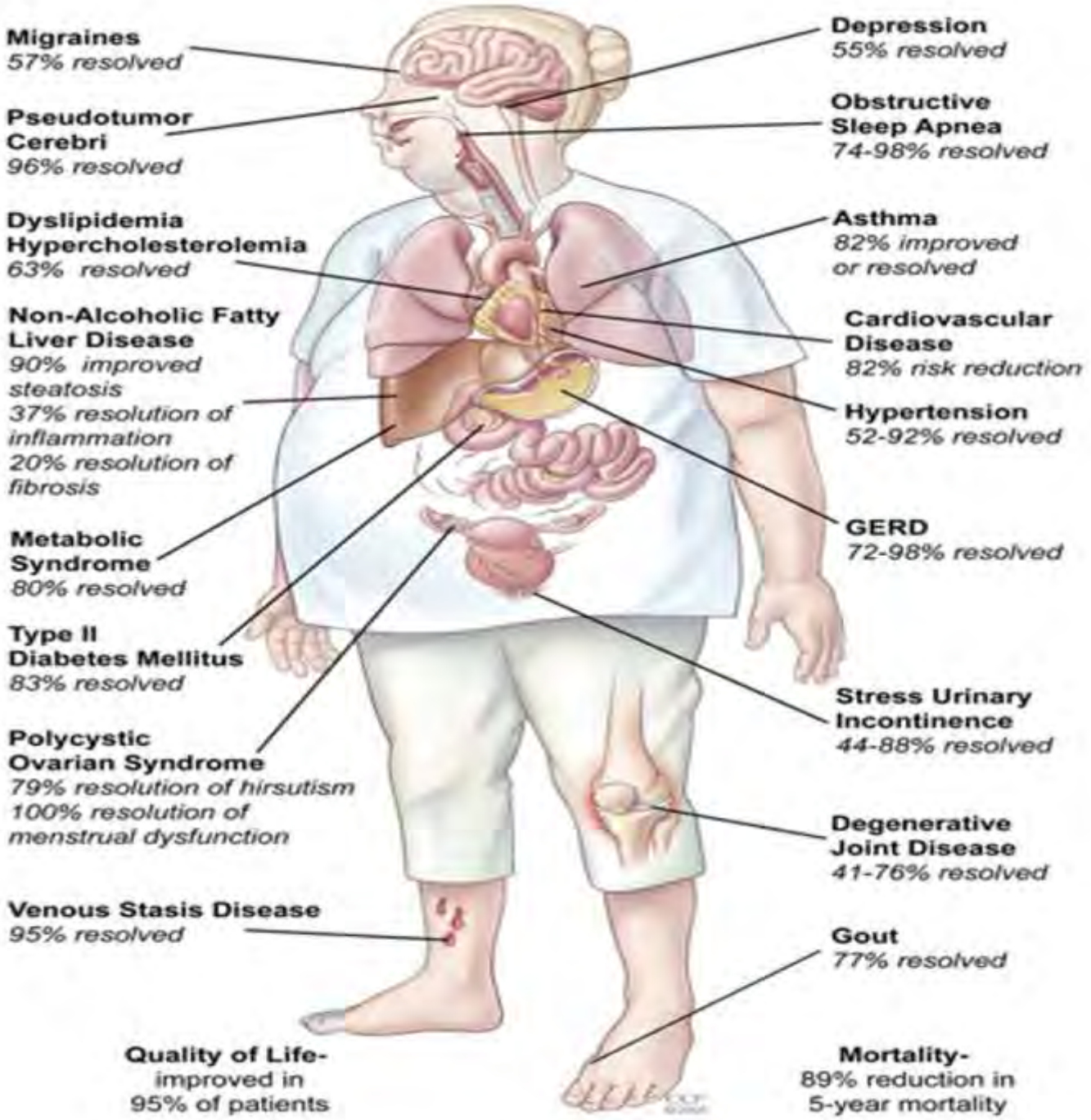
If eat carbs or excessive fat, gas bloating diarrhea.

No dumping.

Increased risk of vitamin deficiencies - need to be on supplementation for life

Weight Loss ~30-35% of total body weight




Migraines
57% resolved
Pseudotumor Cerebri
96% resolved
Dyslipidemia Hypercholesterolemia
63% resolved
Non-Alcoholic Fatty Liver Disease
90% improved steatosis
37% resolution of inflammation
20% resolution of fibrosis
Metabolic Syndrome
80% resolved
Type II Diabetes Mellitus
83% resolved
Polycystic Ovarian Syndrome
79% resolution of hirsutism
100% resolution of menstrual dysfunction
Venous Stasis Disease
95% resolved
Quality of Life-
improved in 95% of patients
Depression
55% resolved
Obstructive Sleep Apnea
74-98% resolved
Asthma
82% improved or resolved
Cardiovascular Disease
82% risk reduction
Hypertension
52-92% resolved
GERD
72-98% resolved
Stress Urinary Incontinence
44-88% resolved
Degenerative Joint Disease
41-76% resolved
Gout
77% resolved
Mortality-
89% reduction in 5-year mortality

JAMA | Original Investigation

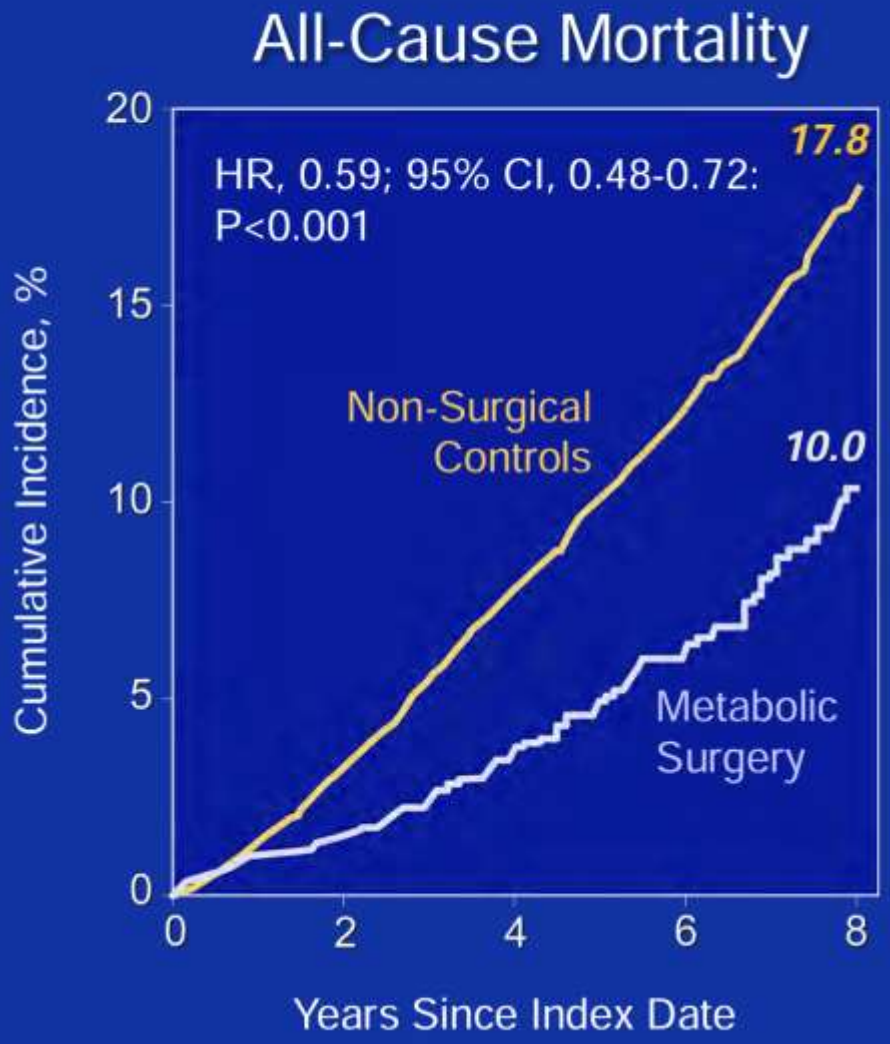
Association of Metabolic Surgery With Major Adverse Cardiovascular Outcomes in Patients With Type 2 Diabetes and Obesity

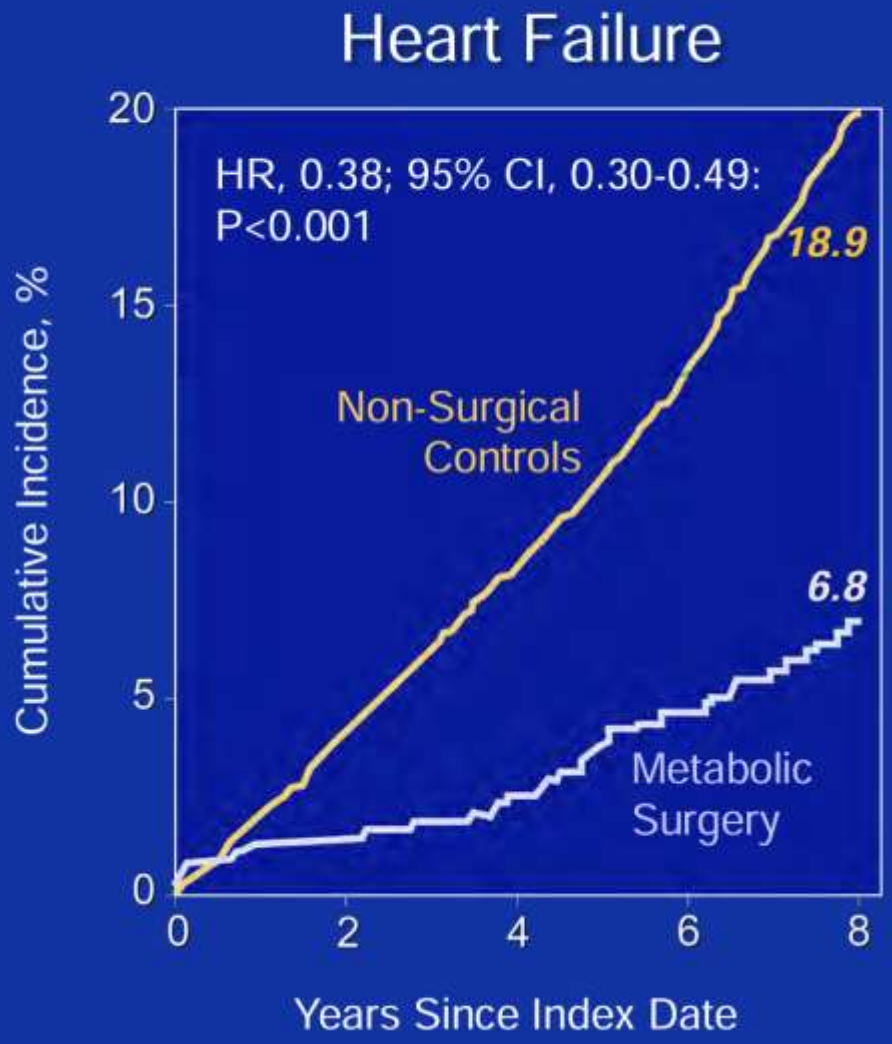
Ali Aminian, MD; Alexander Zajichek, MS; David E. Arterburn, MD, MPH; Kathy E. Wolski, MPH; Stacy A. Brethauer, MD; Philip R. Schauer, MD; Michael W. Kattan, PhD; Steven E. Nissen, MD

2287 Bariatric patients with Type 2 Diabetes mellitus

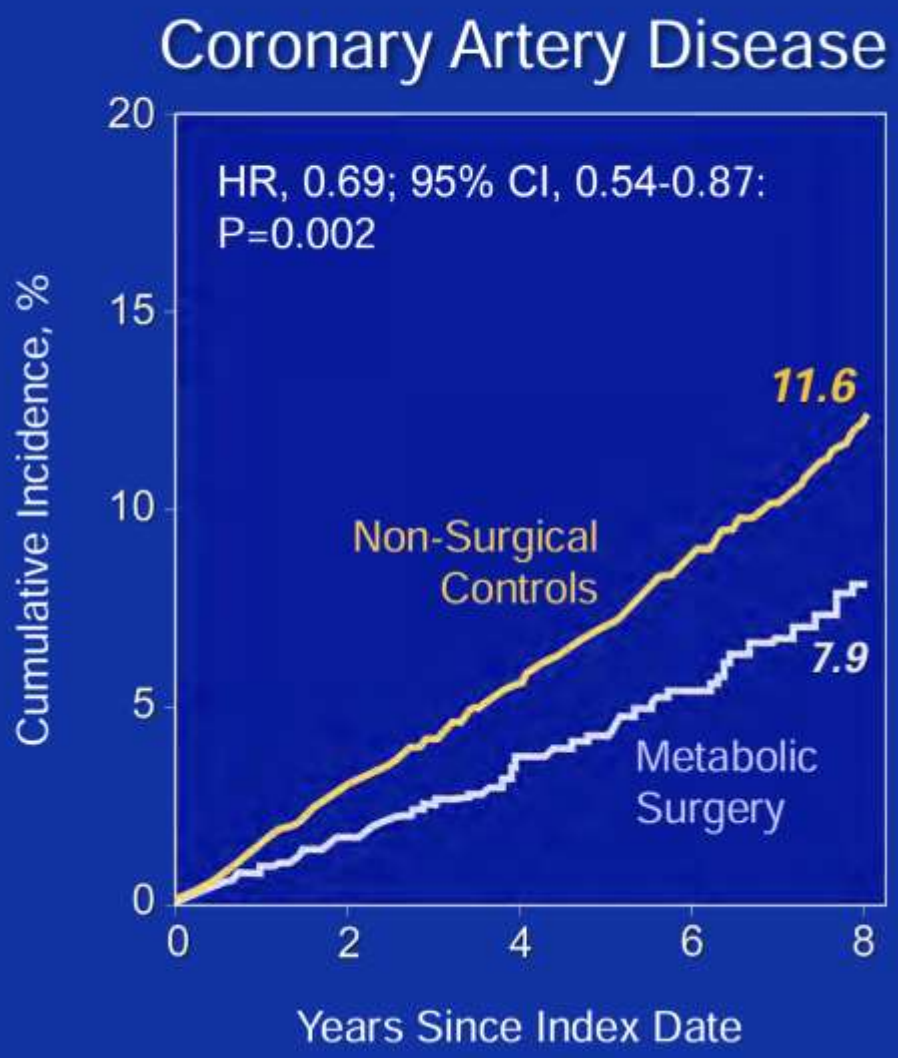
matched 1:5 to 11435 Control patients with Type 2 Diabetes mellitus

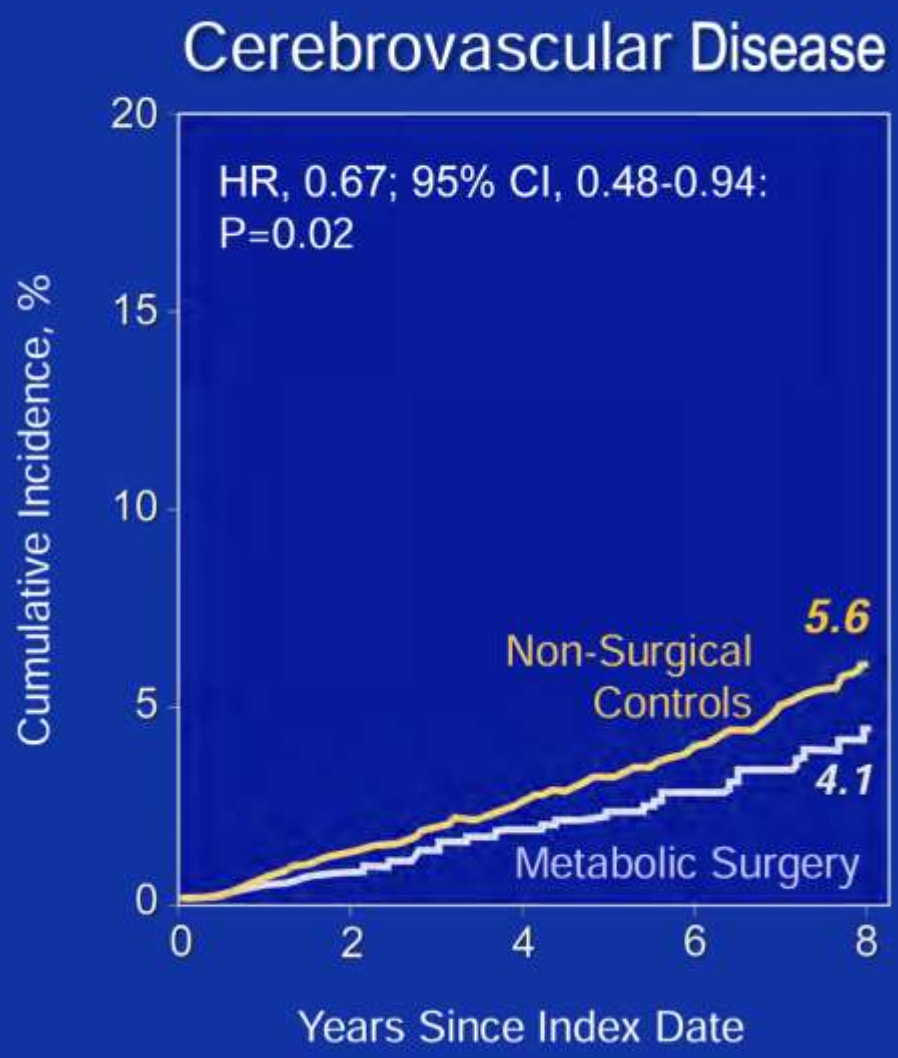
Metabolic Surgery vs. Usual Care



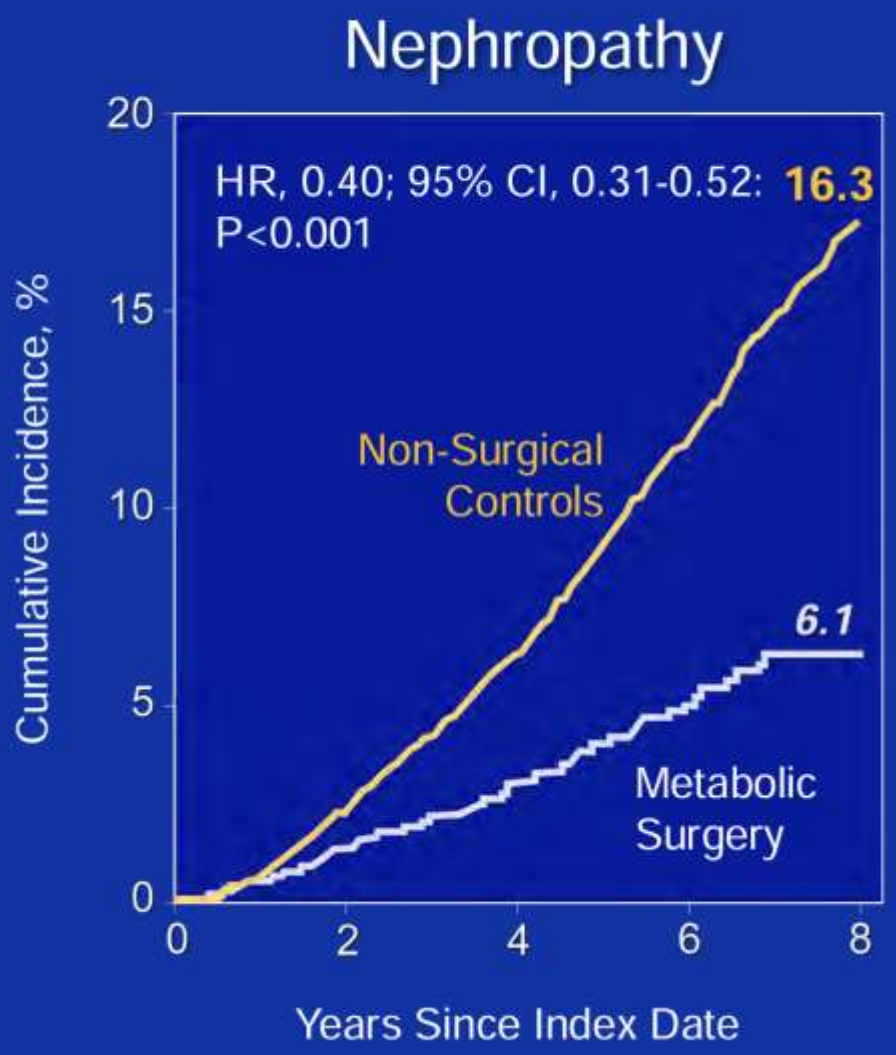


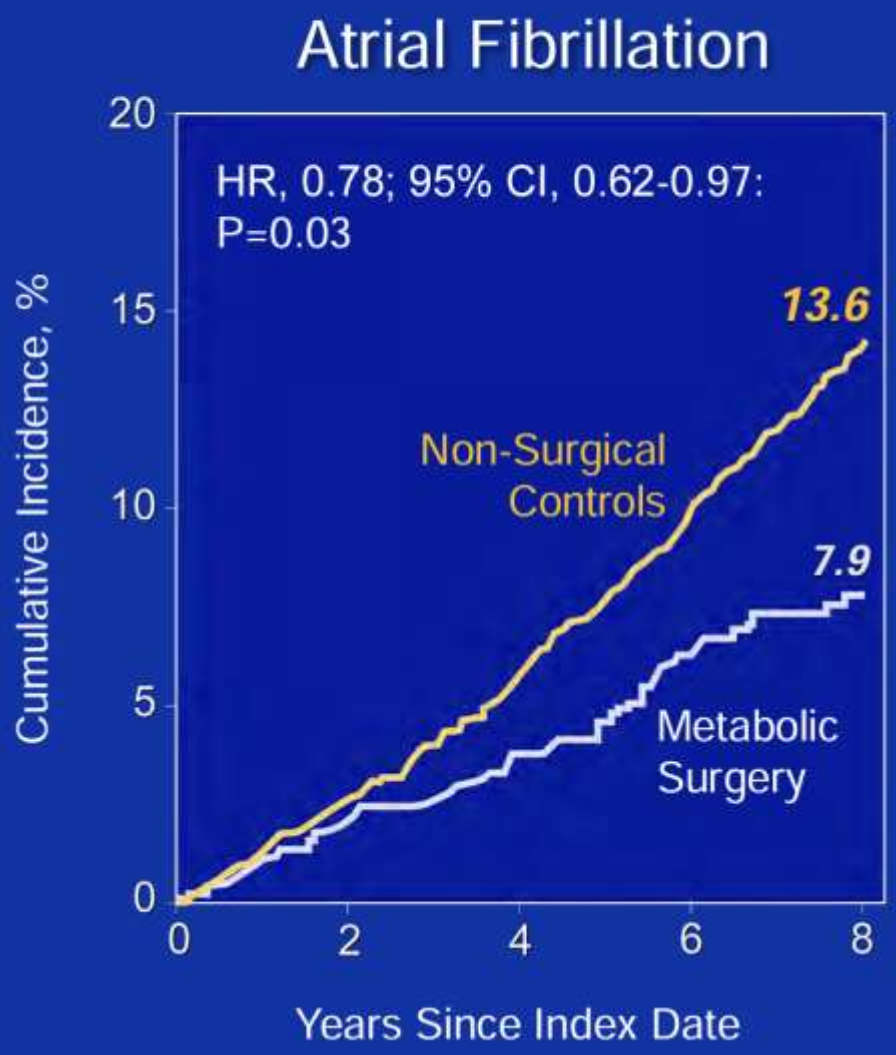
Metabolic Surgery vs. Usual Care





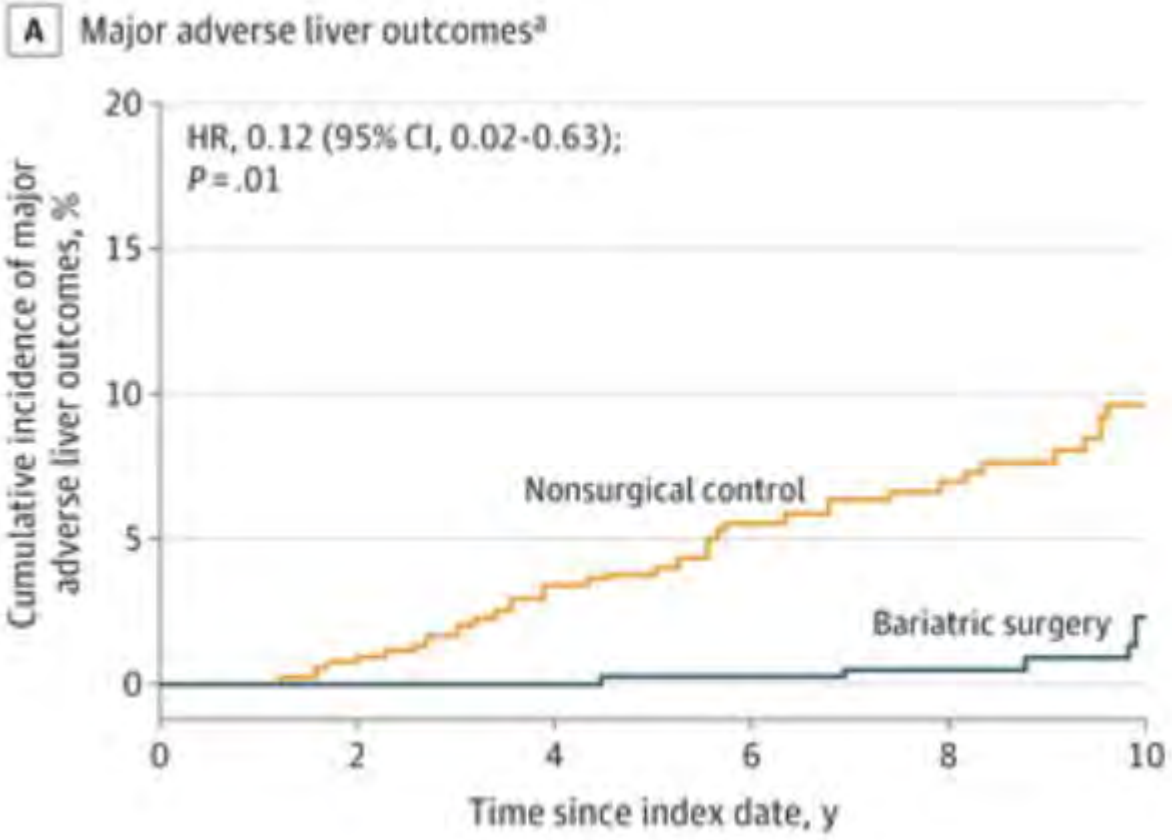
Metabolic Surgery vs. Usual Care





Association of Bariatric Surgery With Major Adverse Liver and Cardiovascular Outcomes in Patients With Biopsy-Proven Nonalcoholic Steatohepatitis

Ali Aminian, MD; Abbas Al-Kurd, MD; Rickesha Wilson, MD; James Bena, MS; Hana Fayazzadeh, MD; Tavankit Singh, MD; Vance L. Albaugh, MD, PhD; Faiz U. Shariff, MD; Noe A. Rodriguez, MD; Jian Jin, MS; Stacy A. Brethauer, MD, MBA; Srinivasan Dasarathy, MD; Naim Alkhouri, MD; Philip R. Schauer, MD; Arthur J. McCullough, MD; Steven E. Nissen, MD



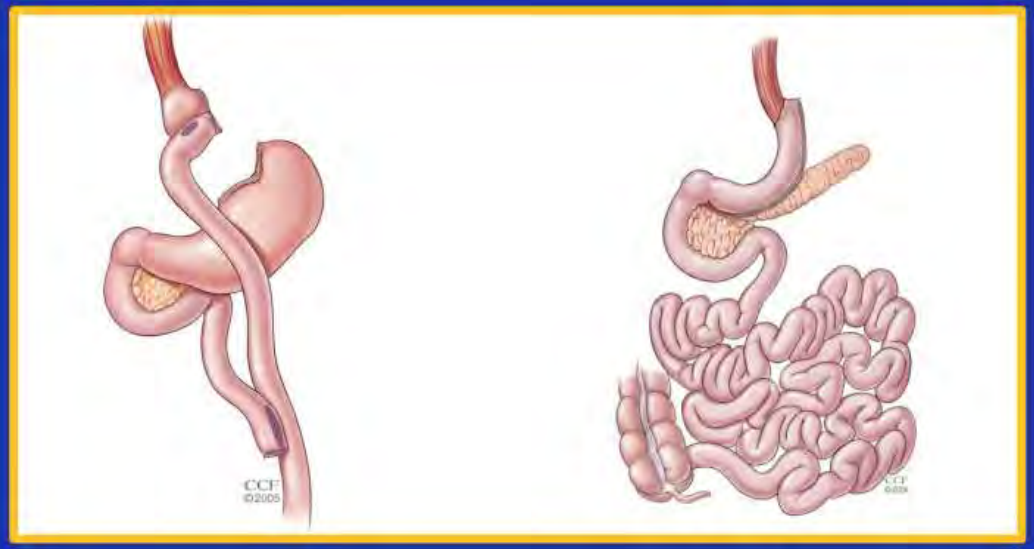
JAMA | Original Investigation

Association of Bariatric Surgery With Cancer Risk and Mortality in Adults With Obesity

Ali Aminian, MD; Rickesha Wilson, MD; Abbas Al-Kurd, MD; Chao Tu, MS; Alex Milinovich, BA; Matthew Kroh, MD; Raul J. Rosenthal, MD; Stacy A. Brethauer, MD; Philip R. Schauer, MD; Michael W. Kattan, PhD; Justin C. Brown, PhD; Nathan A. Berger, MD; Jame Abraham, MD; Steven E. Nissen, MD

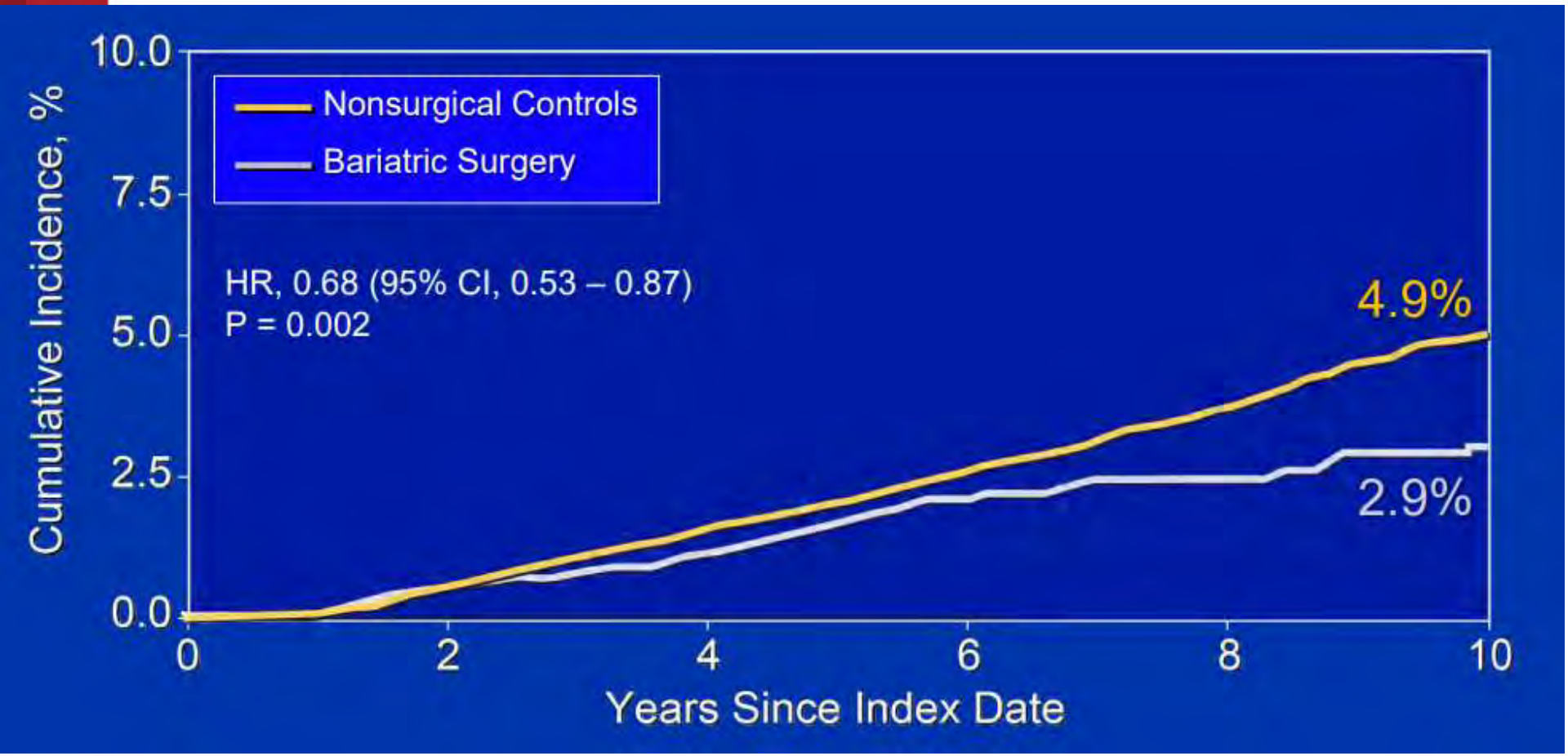
Surgical Procedures and Long-term Effectiveness in Neoplastic Disease Incidence and Death (SPLENDID)

Metabolic Surgical Procedures (N=5053)



Gastric Bypass	Sleeve Gastrectomy
N=3348 (66%)	N=1705 (34%)

Surgical Procedures and Long-term Effectiveness in Neoplastic Disease Incidence and Death (SPLENDID)



Surgical Procedures and Long-term Effectiveness in Neoplastic Disease Incidence and Death (SPLENDID)

The better the weight loss the lower the cumulative risk of cancer

Dose Dependent Response

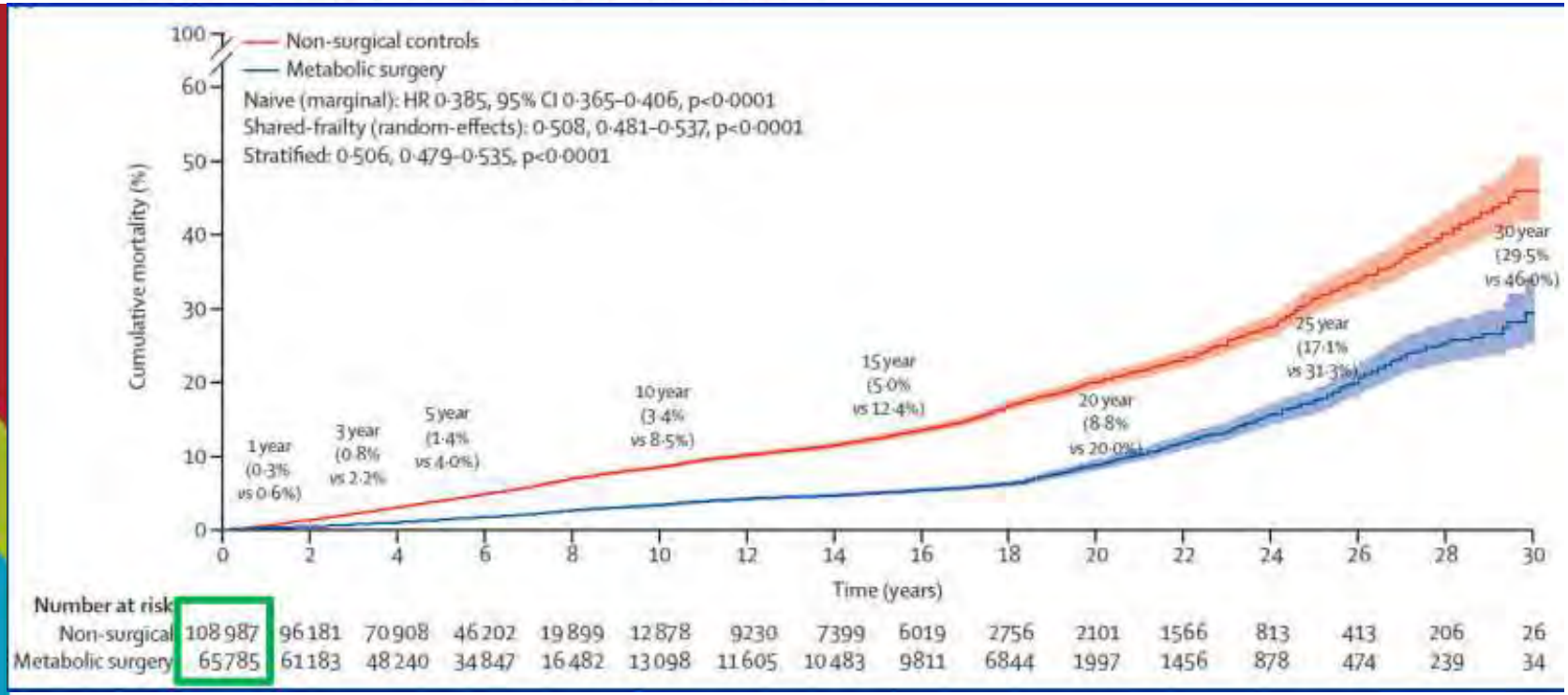
The More the Weight Loss,

The Better the Outcomes

Association of metabolic–bariatric surgery with long-term survival in adults with and without diabetes: a one-stage meta-analysis of matched cohort and prospective controlled studies with 174 772 participants

Nicholas L Syn, David E Cummings*, Louis Z Wang*, Daryl J Lin*, Joseph J Zhao, Marie Loh, Zong Jie Koh, Claire Alexandra Chew, Ying Ern Loo, Bee Choo Tai, Guowei Kim, Jimmy Bok-Yan So, Lee M Kaplan, John B Dixon, Asim Shabbir*

THE LANCET



Median life expectancy gain after surgery:

- Total 6.1 years (95% CI 5.2-6.9)
- Without diabetes: 5.1 years (2.0-9.3)
- With diabetes: 9.3 years (95% CI 7.1-11.8)

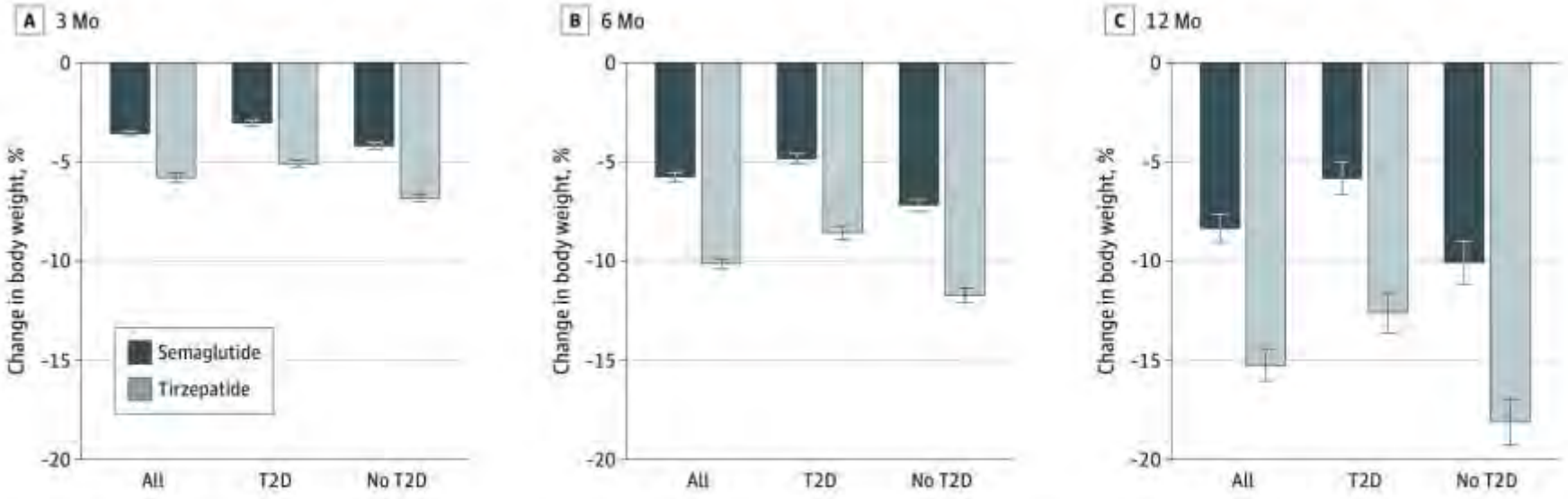
There are no studies that talk about Bariatric Surgery after a primary cancer diagnosis to decrease risk of recurrence or a second primary.

What about Medical Weight Loss in the GLP-1 era?

University of Nebraska Medical Center

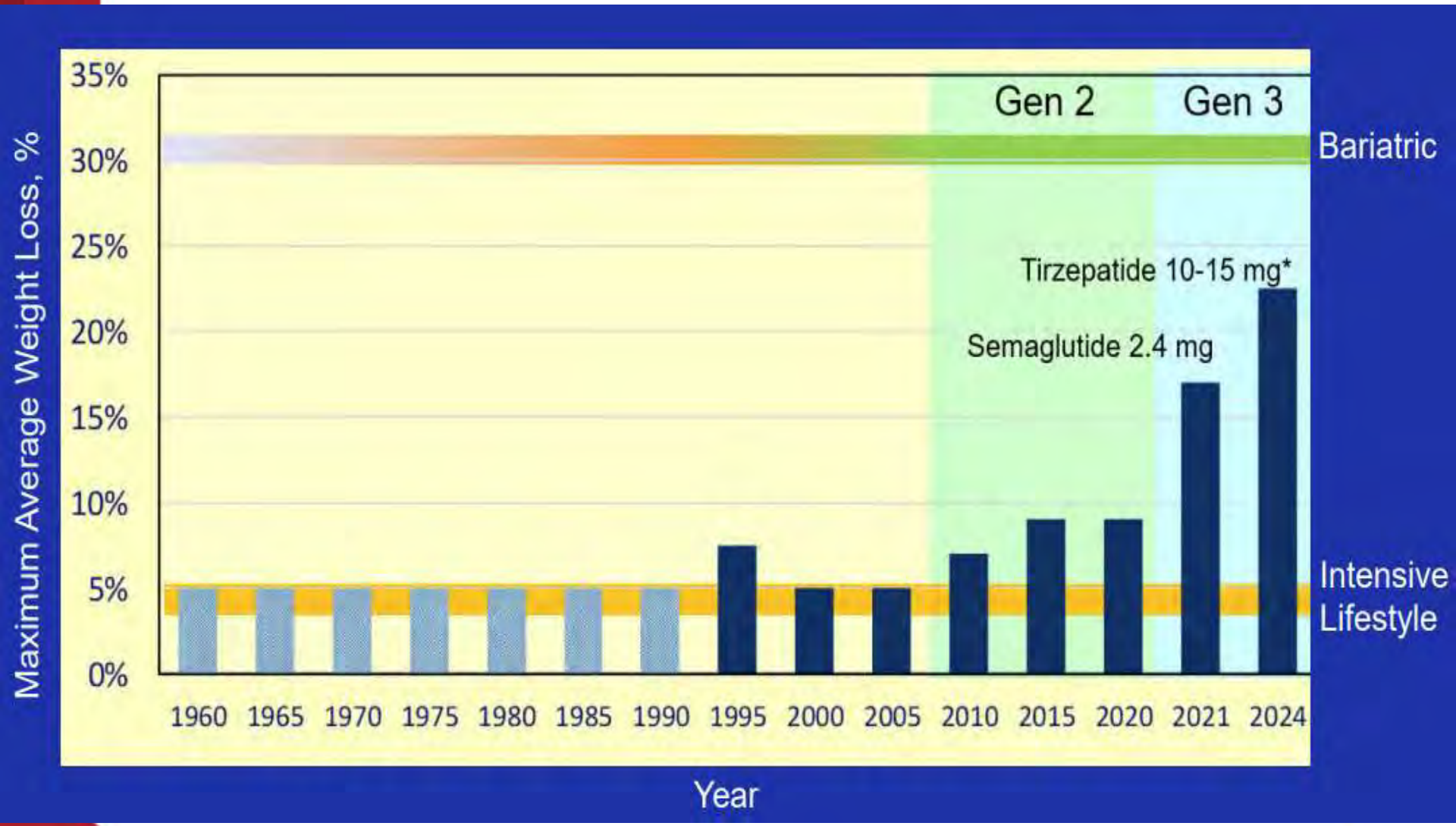
Nebraska Medicine

Semaglutide vs Tirzepatide



Bars represent mean changes in body weight from baseline to the time point among the propensity score matched population of patients still receiving treatment. The whiskers represent 95% CIs.

Obesity Treatment 1960-2024



Kaplan, LM, 2024

Barriers to GLP-1 Therapy

Cost
- Lack of insurance coverage

Supply change issues

Side effects
- Nausea
- Abdominal pain
- Constipation

Contraindications
- Pancreatitis
- MEN 2A or 2B
- Medullary Thyroid Cancer

Impact of Prior Bariatric Surgery on Cancer

University of Nebraska Medical Center

Nebraska Medicine

Gastroesophageal Cancer After Gastric Bypass Surgeries: a Systematic Review and Meta-analysis

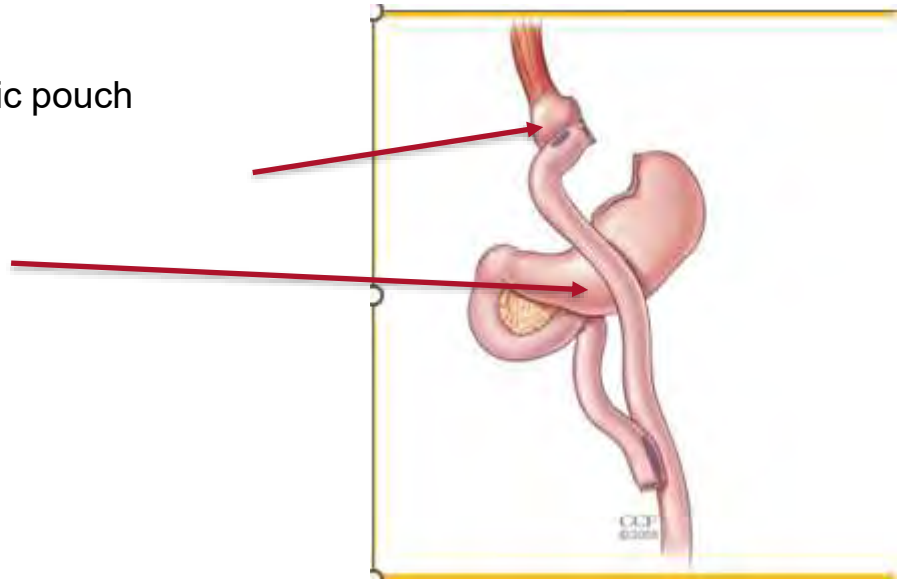
Rodrigue Chemaly[1,2] · Samer Diab[1] · Georges Khazen[3] · Georges Al-Hajj[1,2]

Gastroesophageal adenocarcinoma after gastric bypass.

52 cases identified

30 cancers in the distal esophagus/ gastric pouch

22 cancers in the excluded stomach



Symptoms:

- Abdominal distention (5)
- Abdominal pain (23)
- Anemia(6)
- Anorexia/Early satiety (2)
- Constipation (1)
- Dysphagia (16)
- GERD(1)
- Melena(5)
- N/V(10)
- Weight loss (13

Risk of Esophageal and Gastric Cancer After Bariatric Surgery

Andrea Lazzati, MD, PhD[1,2]; Tigran Poghosyan, MD, PhD[3,4,5]; Marwa Touati, MS[6]; et al

National discharge database in France (PMSI)- 2010-2019

303,709 had bariatric surgery and at least a 2 year follow up with no cancer diagnosis

Matched 1:2 with obese patients who did not have MBS

	MBS	Control	P value
Follow up (years)	6.06	5.62	
Esophageal CA	26	86	
case per 100,000	1.8	2.3	0.05
Gastric cancer	57	168	
case per 100,000	3.3	4.6	0.04
EG CA Total	83	254	
case per 100,000	4.9	6.9	0.005

Therapeutic Challenges

University of Nebraska Medical Center

Nebraska Medicine

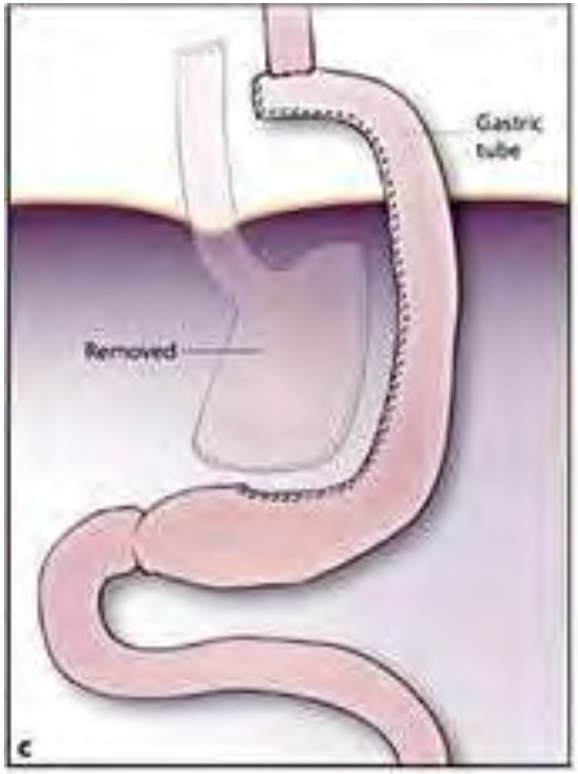
Clinical practice guidelines for the perioperative nutrition, metabolic, and nonsurgical support of patients undergoing bariatric procedures – 2019 update: cosponsored by American Association of Clinical Endocrinologists/American College of Endocrinology, The Obesity Society, American Society for Metabolic & Bariatric Surgery, Obesity Medicine Association, and American Society of Anesthesiologists

2020

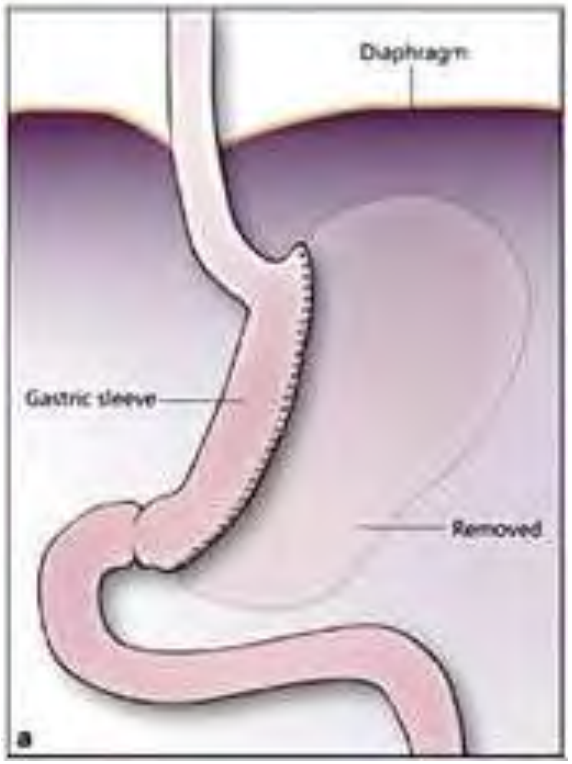
Nutrient	Amount	Risk of deficiency
Protein	60-120 gm/day	1-10%
B1 (thiamine)	50-100 mg daily	<1-49%
B12 (cobalamin)	350-1000 µg daily	RYGB <20%, SG 4-20%
Folate (folic acid)	400-1000 µg daily	65%
Iron	40-60 mg elemental daily	SG <18%, RYGB 20-55%, DS 8-50%
Calcium/Vit D	Ca-1200-2400 mg/d Vit D 3000 IU daily	Up to 100%
Vit A	5000-10000IU/d	DS 70
Vit E	15 mg/d	Uncommon
Vit K	90-300 µg daily	Uncommon
Zinc	8-22 mg daily	SG <19%, RYGB 40%, DS up to 70%%
Copper	1-2 mg daily	RYGB 10-20%, DS up to 90%

Surgery for Obesity and Related Diseases 16 (2020) 175–247

Distal esophagus/GEJ Cancer

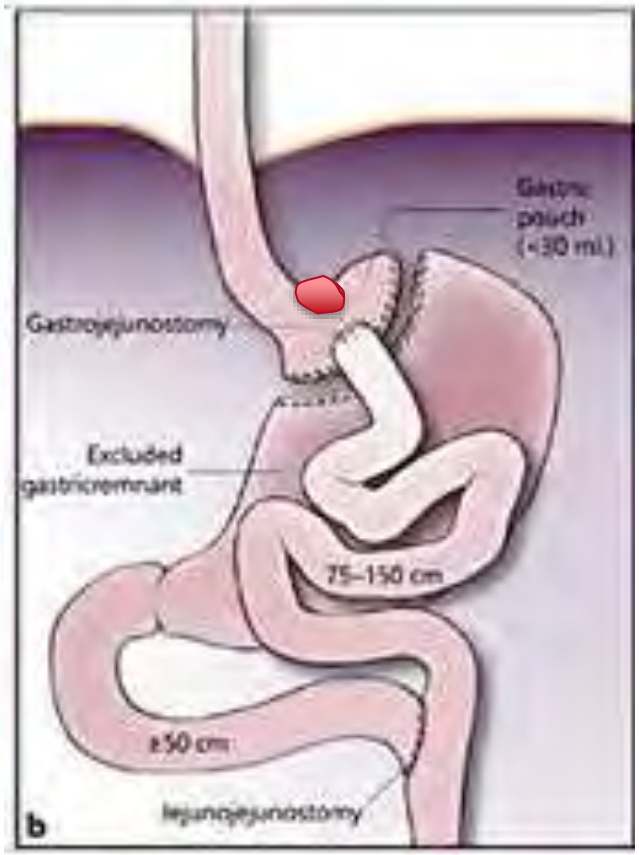


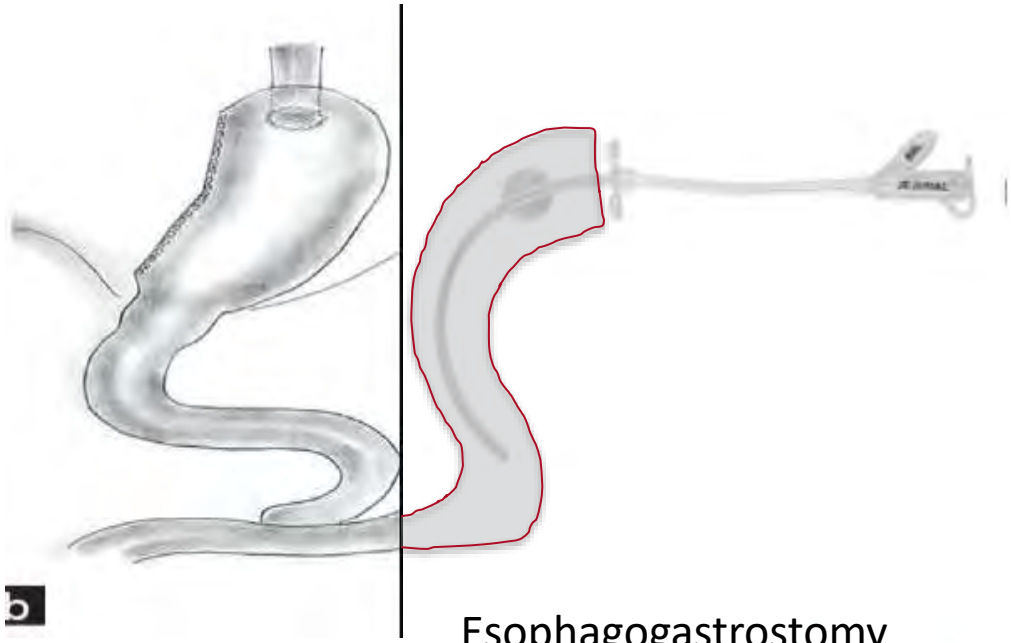
Distal esophagus and proximal stomach resected and gastric tube is created.



All operations that are based on a sleeve gastrectomy had eliminated the gastric tube

Distal esophagus/GEJ Cancer

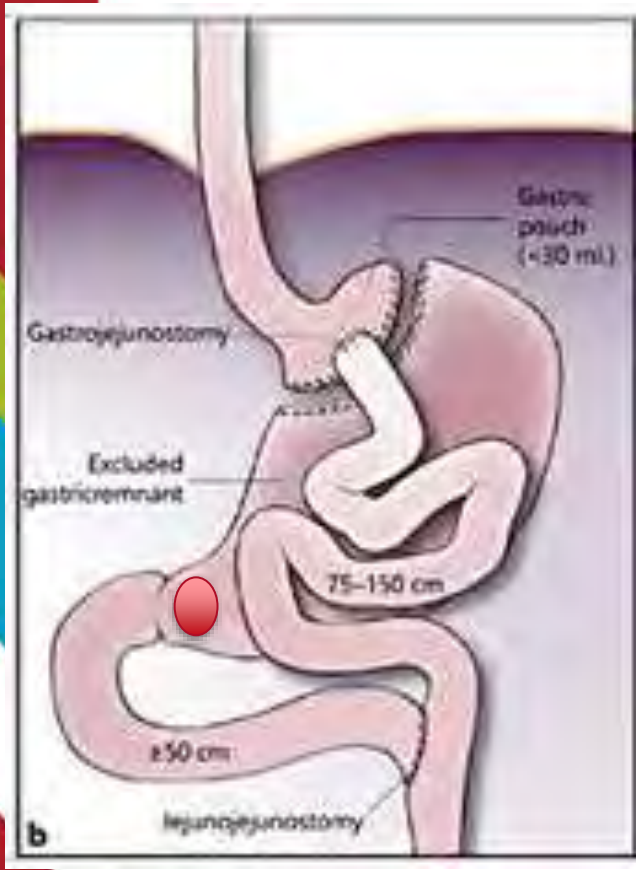


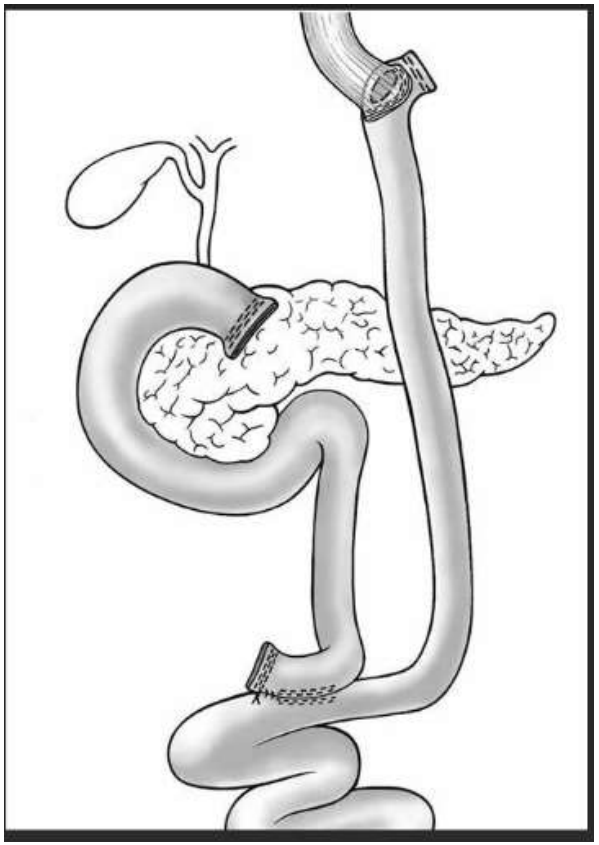


Esophagogastrostomy

With a J tube into the Roux limb

Distal esophagus/GEJ Cancer





Complete gastrectomy

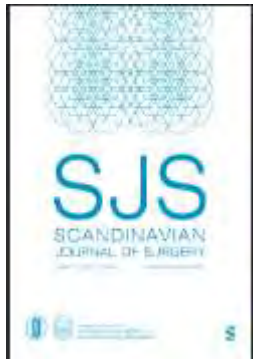
EJ with the pre-existing Roux limb

J tube into biliary limb or common channel

Roux needs to be at least 60-100 cm to prevent bile reflux

Pancreatoduodenectomy after Roux-en-Y gastric bypass surgery: Single-center experience and literature review

Sheraz Yaqub [1], Tore Tholfsen[2], Anne Waage[3], Dyre Kleive[4], and Knut Jørgen Labori[5]



6 patient (788) had a RY Gastric bypass for obesity and later developed pancreatic CA

Presenting symptoms: Pain (50%)
Jaundice (50%)

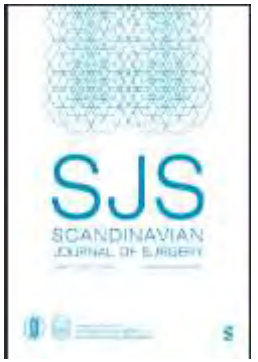
Median 5.5 years after RYGB

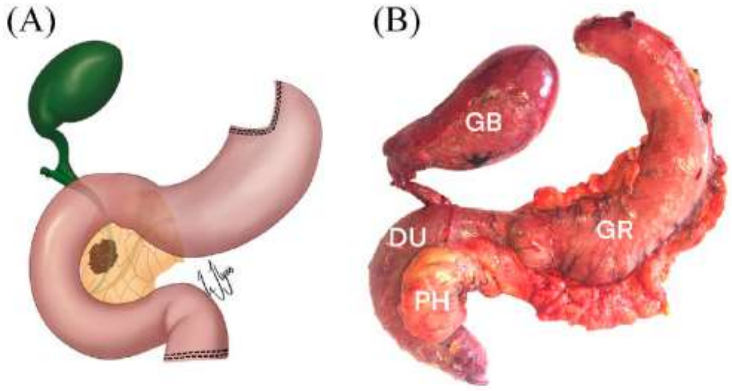
Median follow up 60 mo.

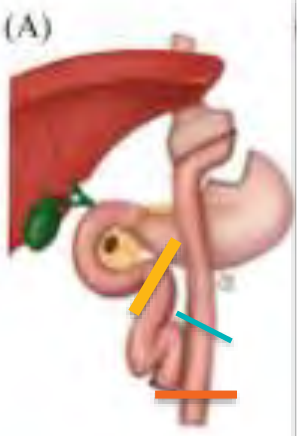
Scandinavian Journal of Surgery
Volume 112, Issue 2, June 2023, Pages 98-104

Pancreatoduodenectomy after Roux-en-Y gastric bypass surgery: Single-center experience and literature review

Sheraz Yaqub [1], Tore Tholfsen[2], Anne Waage[3], Dyre Kleive[4], and Knut Jørgen Labori[5]



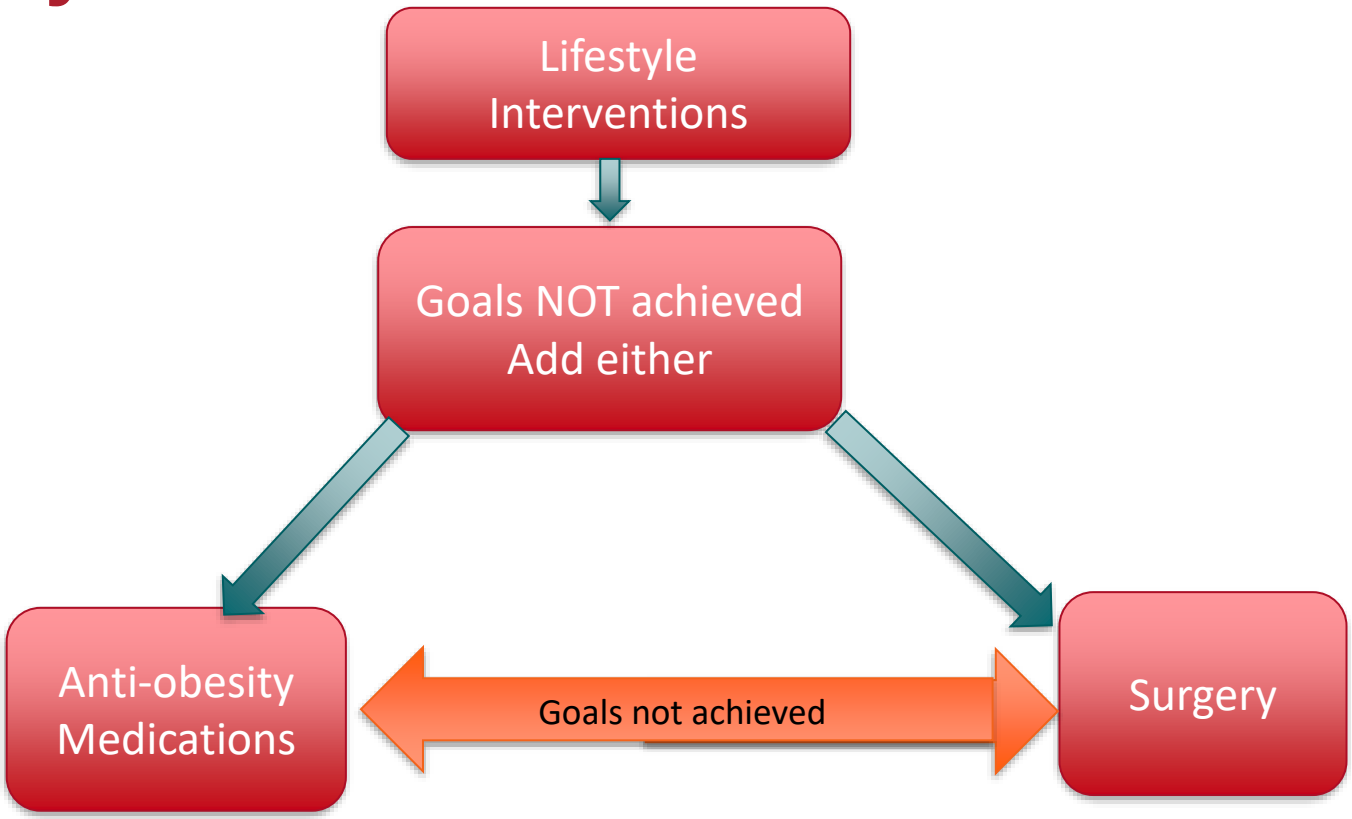




RYGB Anatomy

Scandinavian Journal of Surgery
Volume 112, Issue 2, June 2023, Pages 98-104

Treatment Approach for Obesity



Conclusion

Obesity contributes to mortality

- The higher the BMI the shorter the life expectancy

Obesity is linked to multiple malignancies

- Heavier patients can be more difficult to diagnose, and treat

Obesity related co-morbidities can contribute to complications and long term mortality

Bariatric Surgery decreases the risk of getting and dying of cancer.

Bariatric Medicine and Surgery can decrease the risk of dying of obesity related complications

- Surgery is more effective and cost effective.

University of Nebraska Medical Center

Nebraska Medicine