Cancer Prevention: Weighing In on Weight Loss Shots

Matthew Lunning, DO, FACP
University of Nebraska Medical Center
April 2025

University of Nebraska Medical Center℠

Disclosures

Updated 4/2025	
Research Support	AbbVie FATE Therapeutics; Genentech; BMS; Kite
Consultancy	AbbVie, ADCT, AZ, BMS, FATE, Genentech, Ipsen, Kite, Pfizer, Recordati, Veeva
Employment	NONE
Stock/Equity	NONE
Speakers Bureau	NONE

Learning Objectives

- Understand the relationship between obesity and cancer risk.
- Review current weight loss medications (GLP-1 agonists).
- Evaluate evidence linking weight loss shots to cancer prevention.
- Discuss ethical and clinical implications of widespread use.

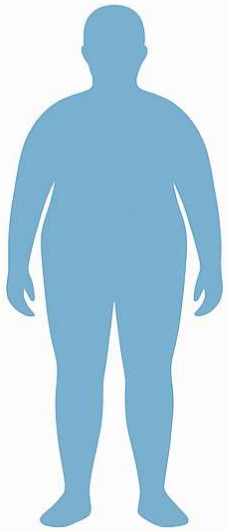
Modifiable Risk Factors

Generated by ChatGPT

Modifiable Risk Factors

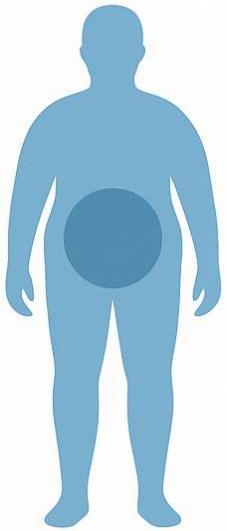
Lifestyle Factor	Associated Cancer(s)	Approximate OR Range
Smoking	Lung, bladder, esophagus, head & neck	**10–30+**
Alcohol	Liver, oral, esophagus, breast	1.5–5
Obesity	Breast, endometrial, colorectal, kidney	1.2–2.5
UV Exposure	Melanoma, squamous/basal cell skin cancer	2–4
HPV (sexual behavior)	Cervical, anal, oropharyngeal	5–100 (varies by subtype)

Defining Obesity



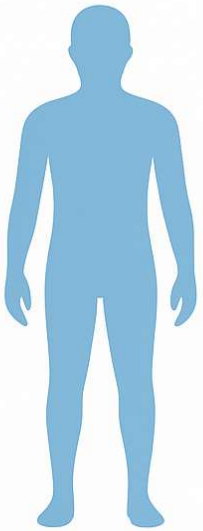
BMI

Measure of weight in relation to height (kg/m^2)



VISCERAL FAT

Excess body fat stored within the abdominal cavity



BODY COMPOSITION

Proportion of fat mass to lean mass

Excess body fat that impairs health

Obesity and Cancer

Chronic Inflammation
Excess adipose tissue promotes a pro-inflammatory state

Hyperinsulinemia
Increased insulin and IGF F-1 levels stimulate cell growth

Increased Estrogen
Aromatase in fat tissue covnverts androgens to estrogens

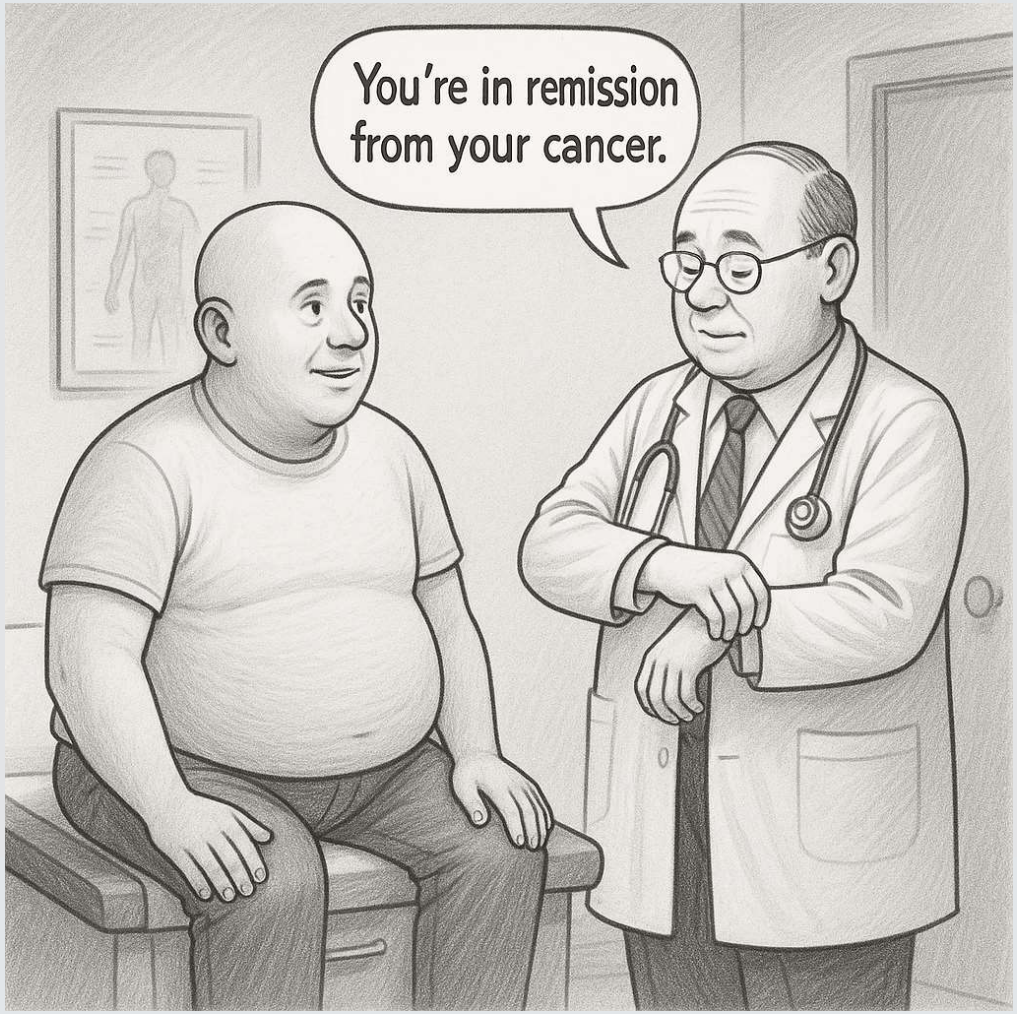
Adipokine Imbalance
Low adiponectin and high leptin affect cell proliferation

Altered Gut Microbiome
Obesity-associated dysbiosis may increase carcinogens

Does Obesity Matter

Generated by ChatGPT

Does This Now Matter



But……Worse Disease-Free Survival

Meyerhardt JA et al., *JNCI*, 2004

Generated by ChatGPT

Treatment Landscape

Lifestyle: Diet and exercise

Pharmacologic: GLP-1s, SGLT2s, others

Surgical: Bariatric procedures

Gila Monster & My Dad

Proliferation of GLP-1

Proliferation of GLP-1

GLP-1 Shaming

Impact	Description
Underreporting to physicians	Patients may avoid disclosing off-label or self-managed use of GLP-1s.
Reduced adherence	Embarrassment or stigma may cause early discontinuation.
Unsafe use	People might obtain medication without proper oversight, labs, or dose titration.
Delayed follow-up	Fear of being judged may prevent timely checkups or monitoring for side effects.

Prevention of Return

Data Generating Phase

TRIM-EBC Trial

Objective: Investigate whether tirzepatide, a GIP/GLP-1 RA, can reduce breast cancer recurrence by lowering or clearing circulating tumor DNA (ctDNA) in overweight or obese patients.

- **Design**: Patients with early-stage breast cancer and detectable ctDNA receive tirzepatide for 24 months.
- **Significance**: This is among the first trials to directly assess a GLP-1 RA's impact on cancer recurrence using ctDNA as a biomarker.

Data Generating Phase

Memorial Sloan Kettering Breast Cancer Cohort Study

- **Objective**: Evaluate weight loss outcomes in breast cancer patients prescribed GLP-1 RAs.
- **Findings**: Among 75 patients, an average weight loss of 5% was observed, with longer treatment durations correlating with greater weight loss.
- **Implications**: While weight loss was achieved, further research is needed to determine the effect on cancer recurrence.

Shen et al. JCO 2024

Data Generating Phase

Northwestern Medicine Retrospective Study

- **Objective**: Assess associations between GLP-1 inhibitor use, cancer recurrence, and all-cause mortality among cancer survivors.
- **Findings**: GLP-1 inhibitor use was linked to a significant reduction in all-cause mortality (HR 0.36) among cancer survivors, though no significant association with cancer recurrence was found.

Chen et al. Cancer Research 2023

GLP-1 Inhibitor Cancer Concerns

Thyroid C-cell Tumors (Rodent Studies)

- All GLP-1 RAs carry a **black box warning** for:
  - "Risk of thyroid C-cell tumors, including medullary thyroid carcinoma (MTC)"
  - No proven link in humans

Contraindicated in:

- Personal or family history of **Medullary Thyroid Cancer (MTC)**
- History of **MEN2 (Multiple Endocrine Neoplasia Type 2)**

USPI

Multi-pronged Approach

Generated by ChatGPT

Key Takeaways

- Obesity increases cancer risk.
- GLP-1s offer effective weight loss.
- Cancer prevention is plausible, but the evidence is early.
- Clinical trials looking at a reduction of cancer recurrence are ongoing in “high-risk cancers.”

University of Nebraska Medical Center