



# UNDERSTANDING UPPER GI MALIGNANCIES

JP MCGHIE / MEDICAL ONCOLOGIST



# DISCLOSURES

- I HAVE RECEIVED SPEAKERS HONORARIA/CONSULTING FEES FROM THE FOLLOWING COMPANIES:
  - AMGEN
  - CELGENE
  - IPSEN
  - TAIHO
- I HAVE AND CONTINUE TO PARTICIPATE IN CLINICAL TRIALS, MANY OF WHICH ARE SUPPORTED BY INDUSTRY FUNDS
- I HAVE REQUESTED/RECEIVED FUNDS FROM SEVERAL COMPANIES TO SUPPORT OUR CONFERENCE (VANCOUVER ISLAND ONCOLOGY CONFERENCE)



A detailed 3D rendering of numerous red blood cells, showing their characteristic biconcave disc shape. The cells are densely packed and appear to be floating in a fluid medium, with a warm red color palette. The lighting creates highlights and shadows, giving the cells a three-dimensional appearance.

**Save the Date!!  
May 8-9, 2020**

**We're Out For Blood!**



# FAIR USE

- THE PRINCIPLES OF “FAIR USE” HAVE BEEN APPLIED TO ALL MATERIALS USED IN THIS PRESENTATION.



# IMMORTALIZED BY FILM, MORTALIZED BY ESOPHAGEAL CANCER

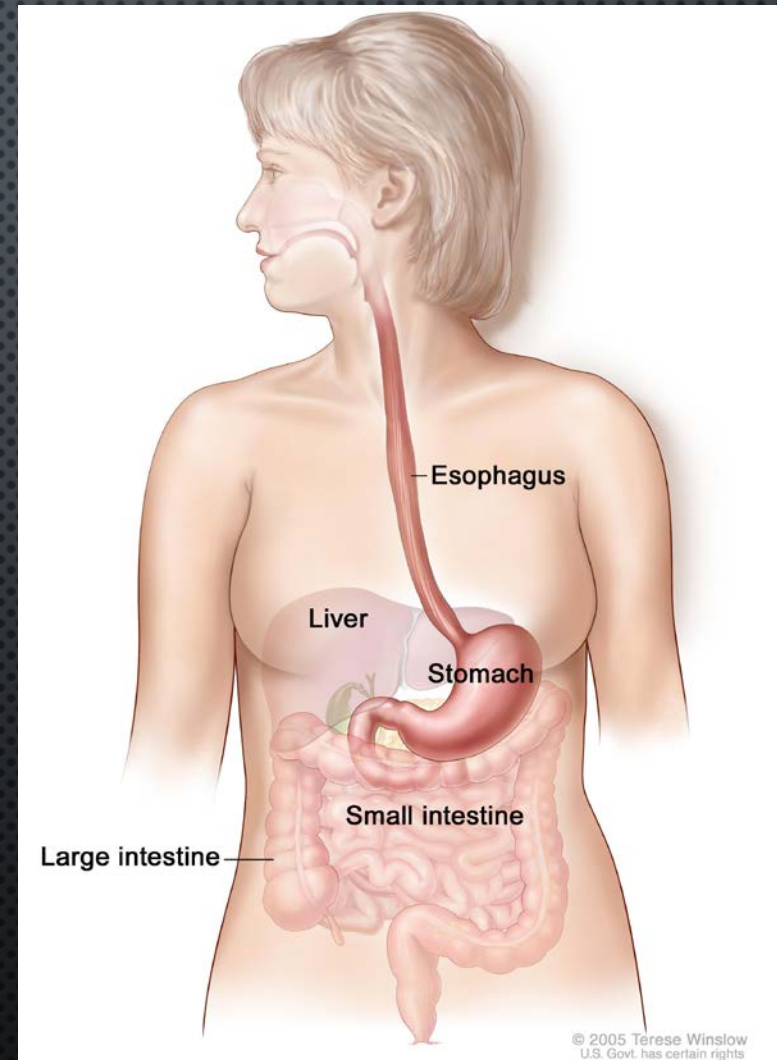
- HUMPHREY DEFOREST BOGART, SUFFERED A COUGH AND DYSPHAGIA IN 1950'S
- SOUGHT MEDICAL ATTENTION IN JANUARY 1956
- DIAGNOSED AND TREATED FOR ESOPHAGEAL CANCER IN MARCH
- DIED IN JANUARY 1957





# OUR PLAN

- YOUR OBJECTIVES / MY GOALS
- INTRODUCTION TO UPPER GI MALIGNANCIES (WORLD / BC)
- SITE 1: ESOPHAGEAL
- SITE 2: GASTRIC
- SITE 3: SMALL BOWEL
- RECAP





# OBJECTIVES



- FOLLOWING THIS PRESENTATION, YOU WILL BE ABLE TO....
  1. DISCUSS THE EPIDEMIOLOGY AND ETIOLOGY OF UPPER GI MALIGNANCIES
  2. IDENTIFY PRESENTING SYMPTOMS OF UPPER GI MALIGNANCIES
  3. DESCRIBE OUR CURRENT TREATMENT APPROACH FOR THESE CANCERS
  4. DISCUSS FOLLOW UP AFTER TREATMENT OF THESE CANCERS WITH YOUR PATIENTS



# MY GOALS...

- YOU CAN IMAGINE THAT THIS IS YOUR DIAGNOSIS...
- YOU CAN DECIDE HOW YOU WOULD FEEL...
- YOU CAN (BETTER) DISCUSS THESE DIAGNOSES AND TREATMENTS WITH YOUR PATIENTS...



Sinclair Scores 180<sup>th</sup> Goal!!!!!!

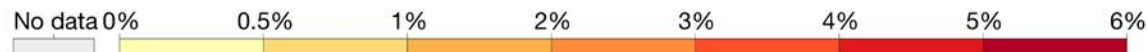
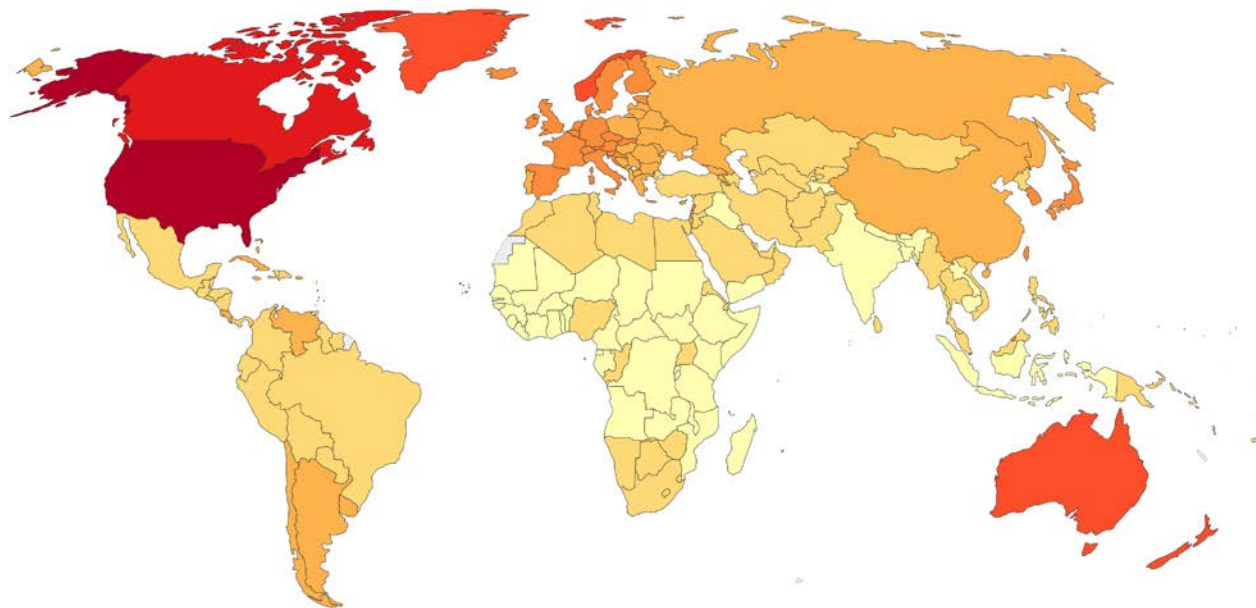


# INTRODUCTION TO UPPER GI MALIGNANCIES

## Share of population with cancer, 2017

Share of total population with any form of cancer, measured as the age-standardized percentage. This share has been age-standardized assuming a constant age structure to compare prevalence between countries and through time.

Our World  
in Data



Source: IHME, Global Burden of Disease

CC BY

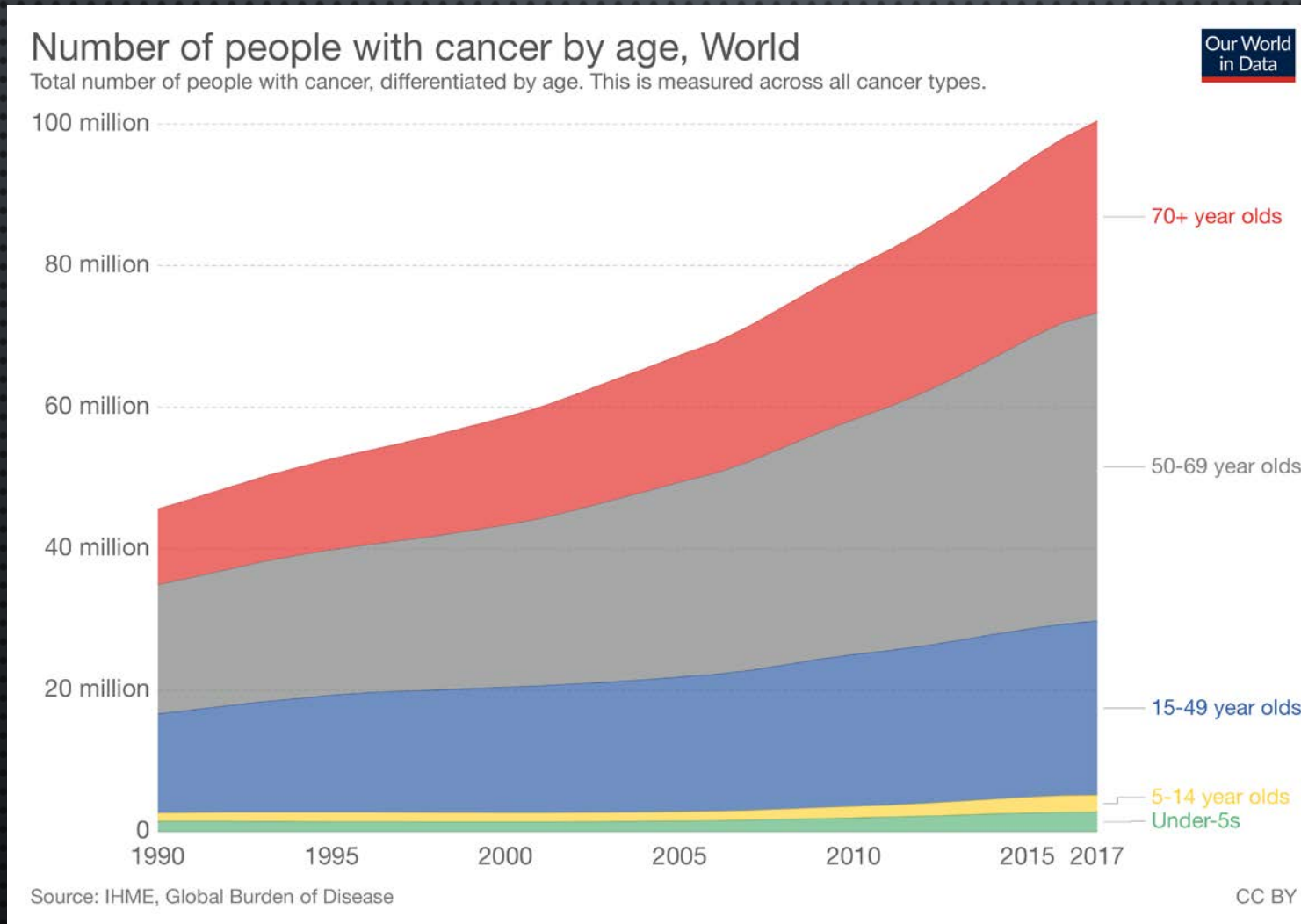
Max Roser and Hannah Ritchie  
(2019) - "Cancer".

Published online at  
[OurWorldInData.org](https://ourworldindata.org).

Retrieved from:  
'<https://ourworldindata.org/cancer>'  
[Online Resource]



# INTRODUCTION TO UPPER GI MALIGNANCIES



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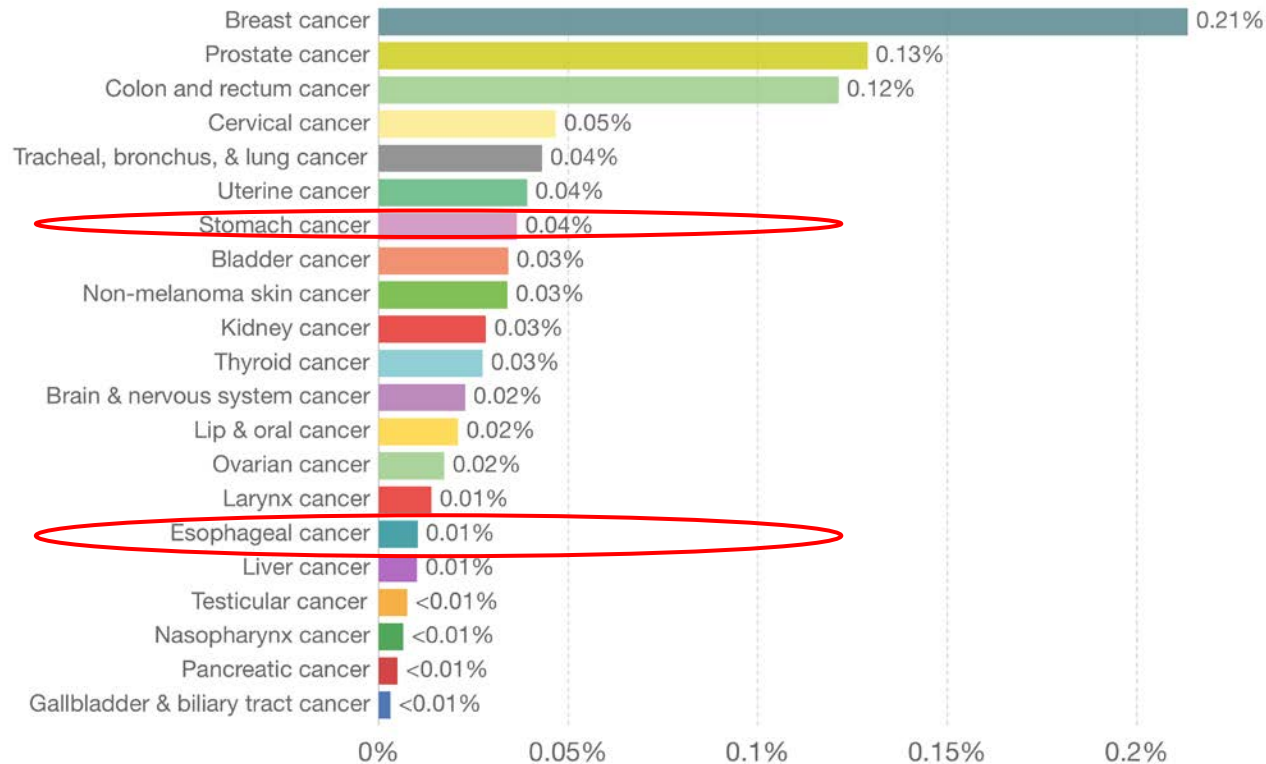


# INTRODUCTION TO UPPER GI MALIGNANCIES

## Share of population with cancer types, World, 2017

Share of total population with different types of cancer over time, measured as the age-standardized percentage. This share has been age-standardized assuming a constant age structure to compare prevalence between countries and through time.

Our World  
in Data



Source: IHME, Global Burden of Disease

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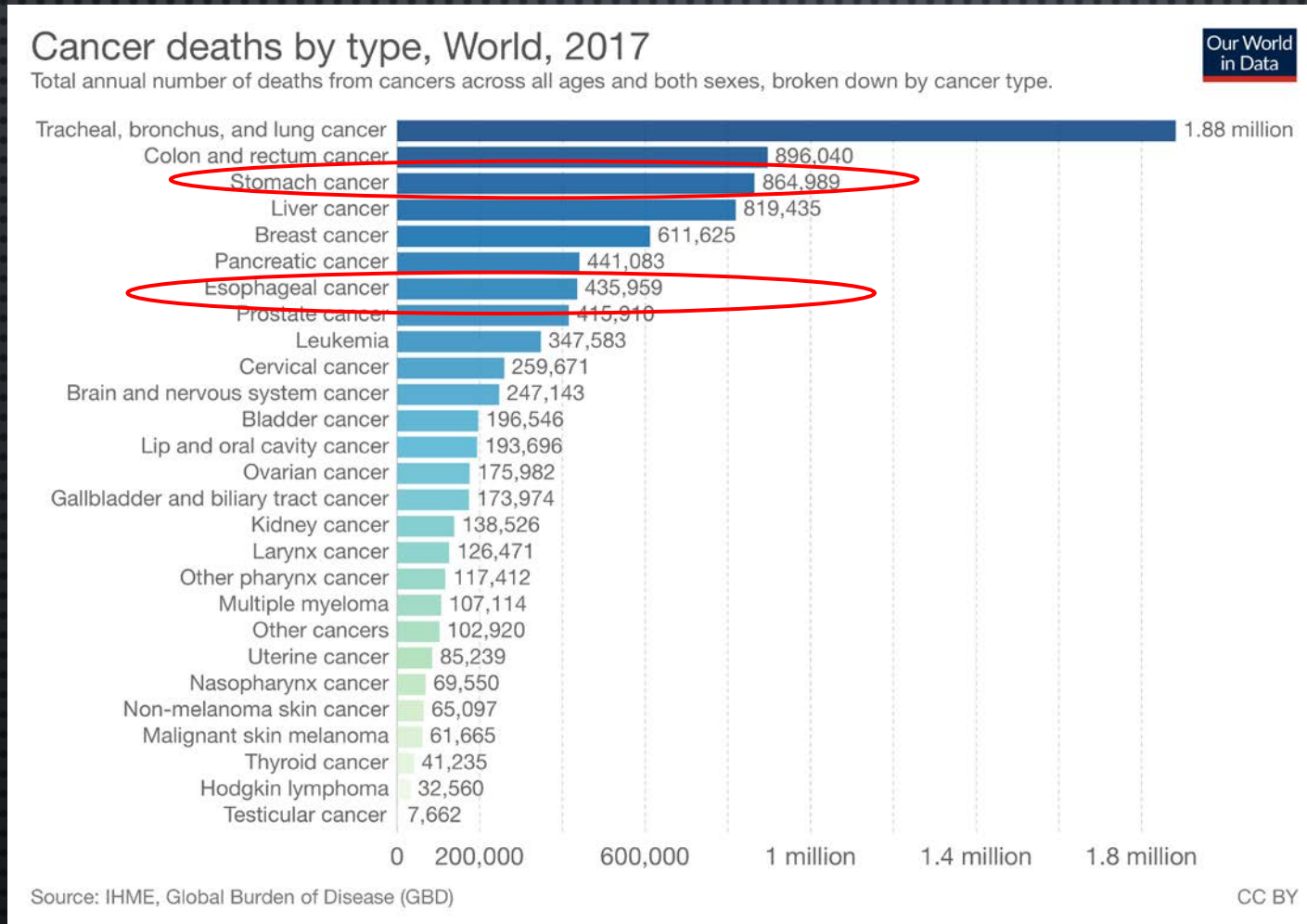
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# INTRODUCTION TO UPPER GI MALIGNANCIES

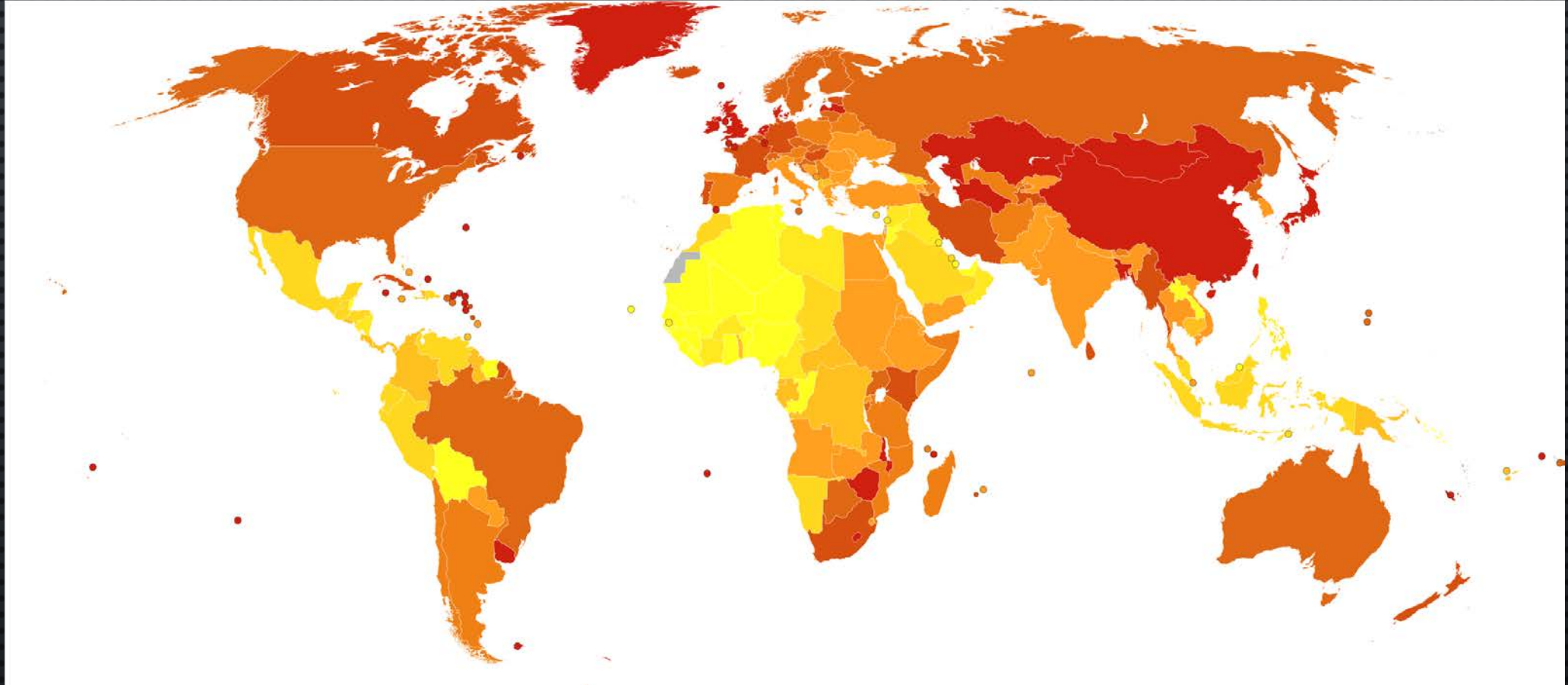


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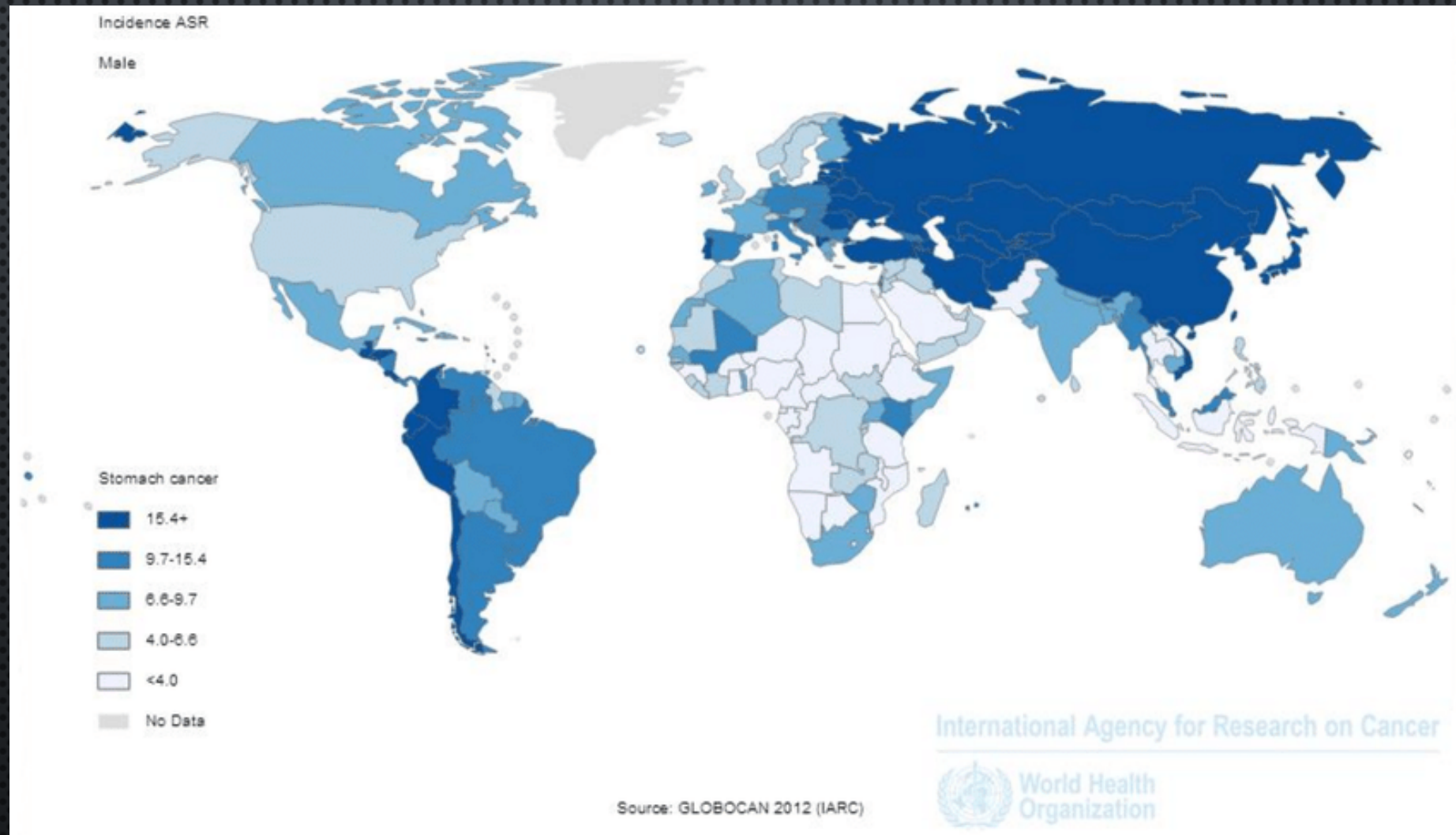
Retrieved from:  
'<https://ourworldindata.org/cancer>'  
[Online Resource]





Esophageal cancer kills millions worldwide





Gastric cancer is a global issue



## HERE IN BC...

Disease Site	Incidence (per 100 000)
Colon + Rectum	66
Esophagus	10
Stomach	11
Small Intestine	2.5

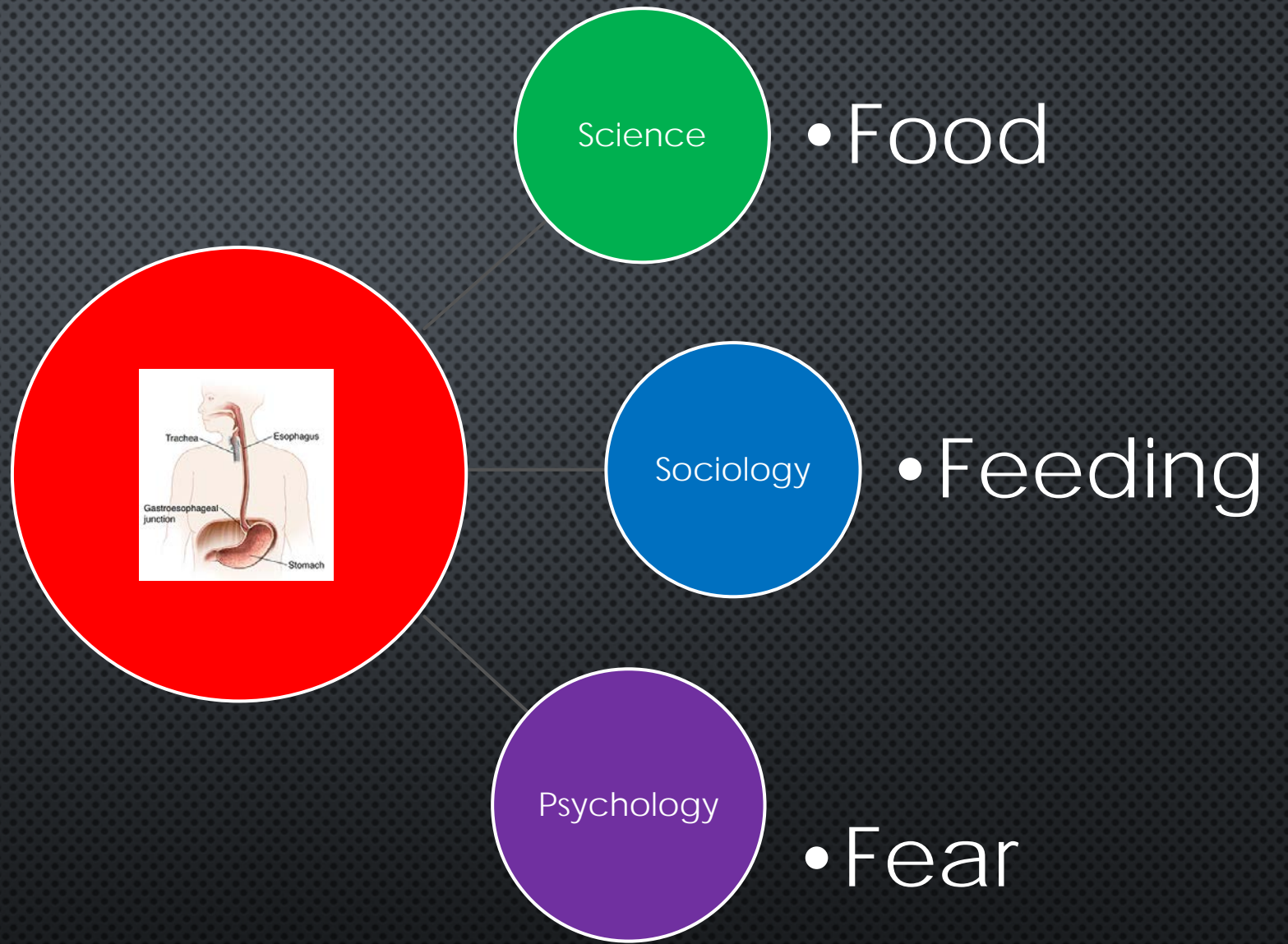
From [bccancer.bc.ca](http://bccancer.bc.ca) (2016)



# QUESTION

- SHOULD OUR COMMUNITY INVEST IN THE GLOBAL HEALTH BURDEN OF THESE DISEASES?
  - **YES**
  - **NO**





# THE COMPLEXITY OF UPPER GI MALIGNANCIES



Science

Eat real food!



Sociology



Feeding is what we do!



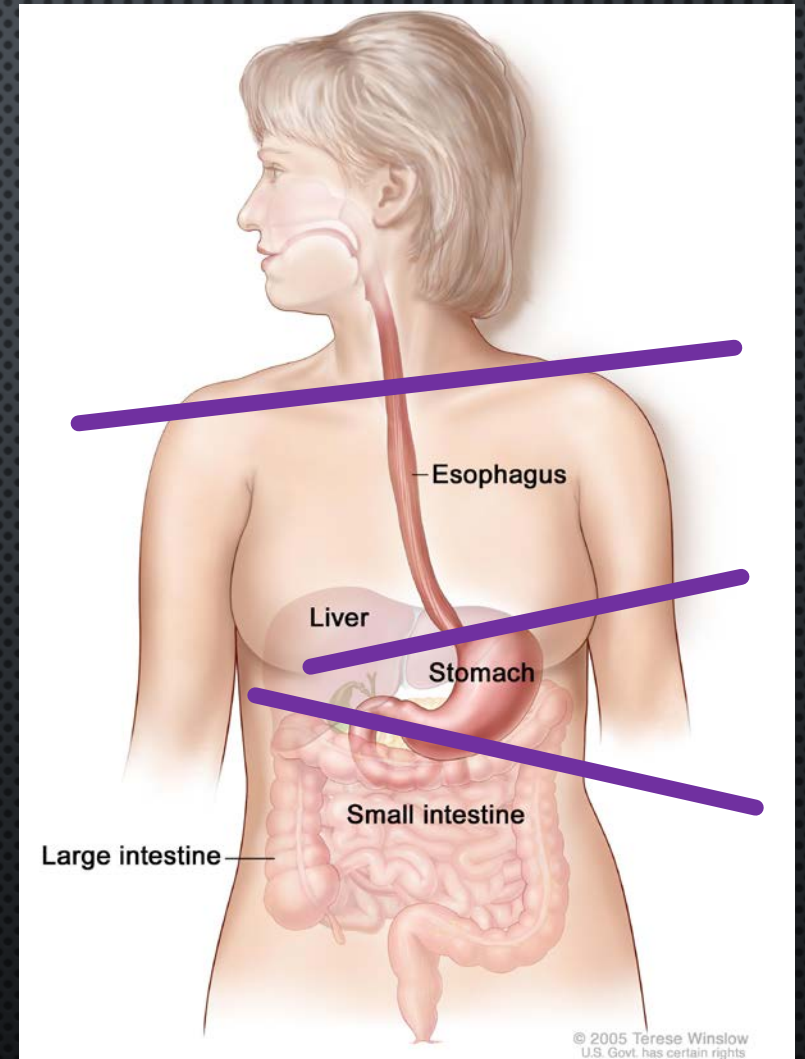
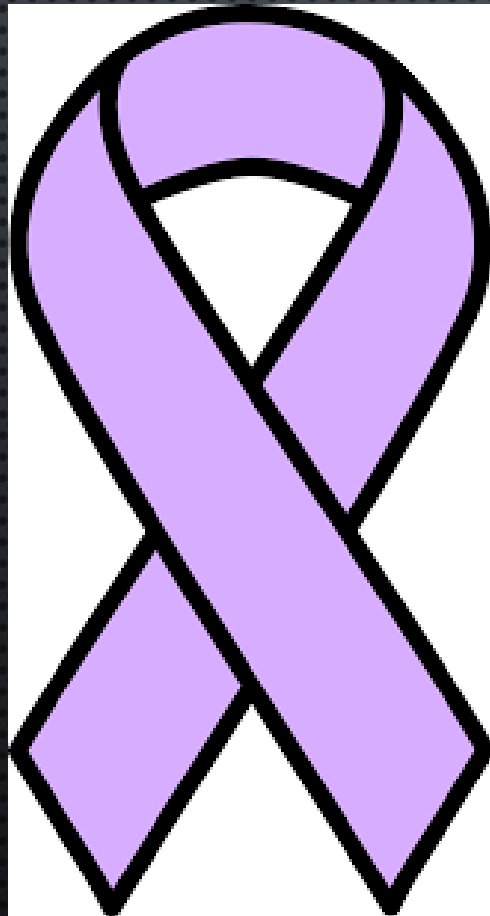
Psychology



All bets are off...



# “DIVISIONS” OF THE GI TRACT...





# ESOPHAGEAL CANCER

## “RICHARD”

- RICHARD CAME TO SEE ME IN 2016...
- AFTER MANY MONTHS OF SWALLOWING DIFFICULTIES...
- THE WEIGHT LOSS WAS ALARMING

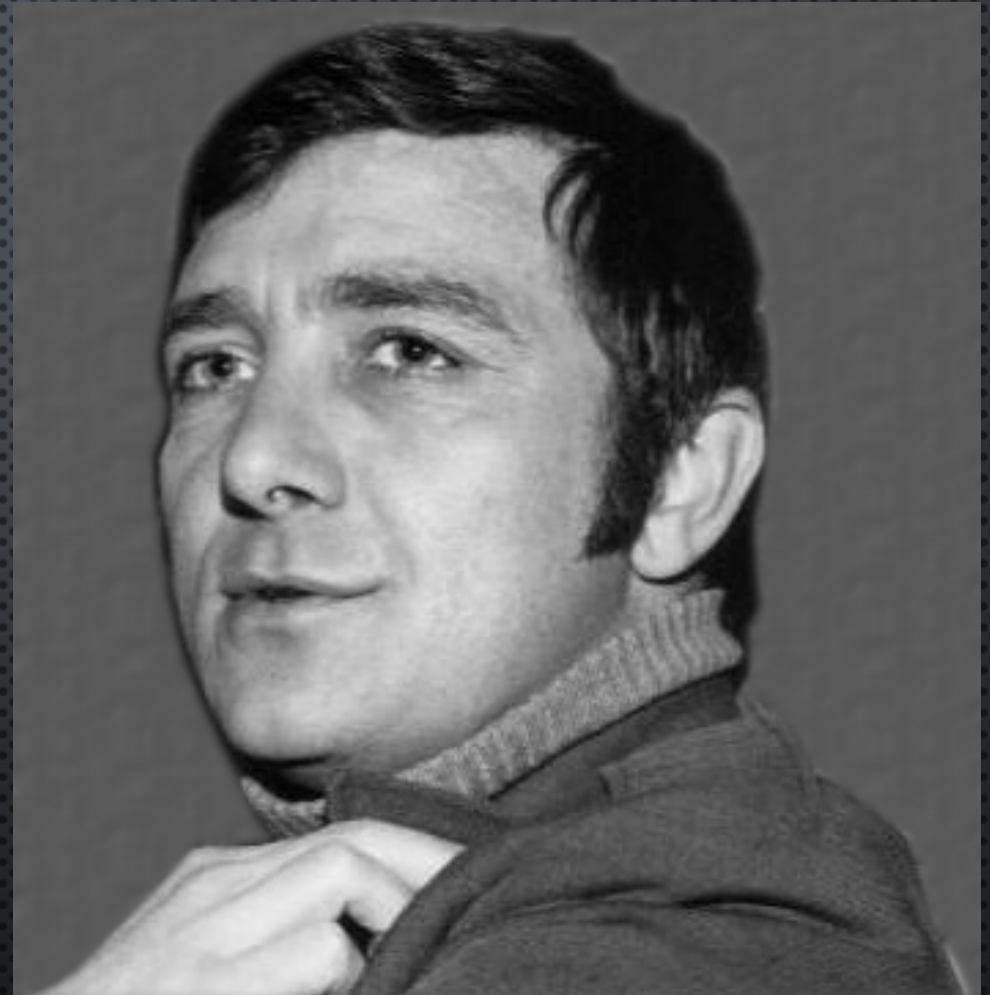
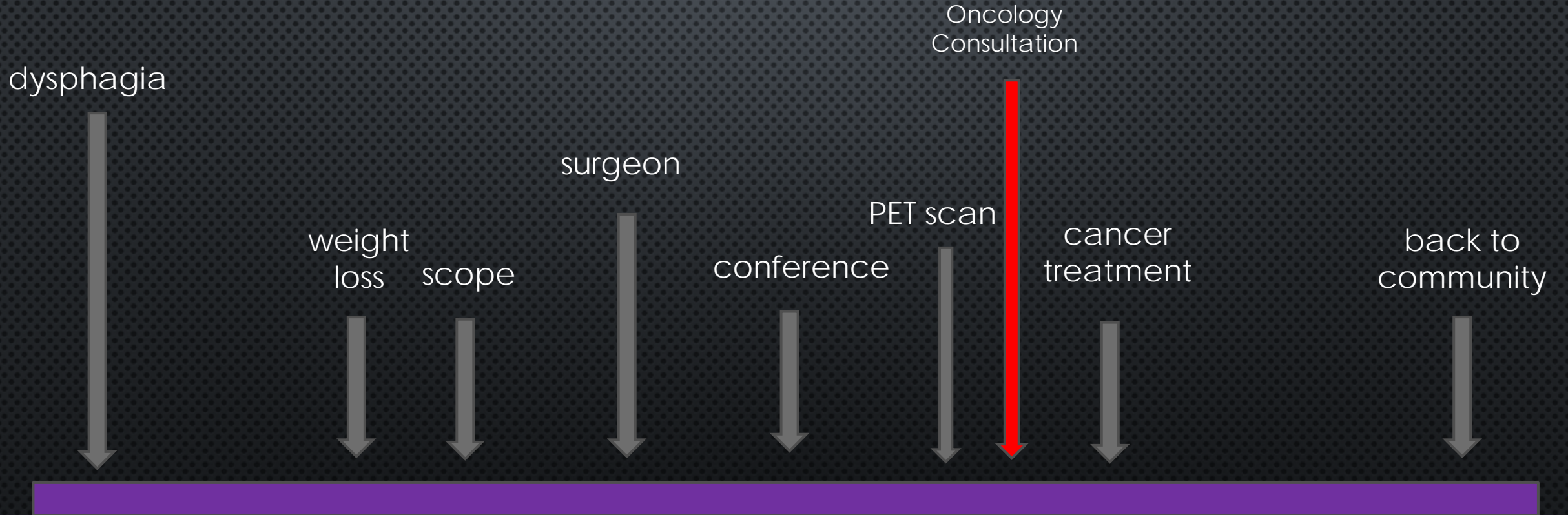


Photo from wikipedia



# RICHARD'S TIMELINE





HOW WOULD YOU DESCRIBE YOUR BEHAVIOR IF  
THIS WAS YOUR TIMELINE?

Calm

Just Barely Coping

Crazy



1

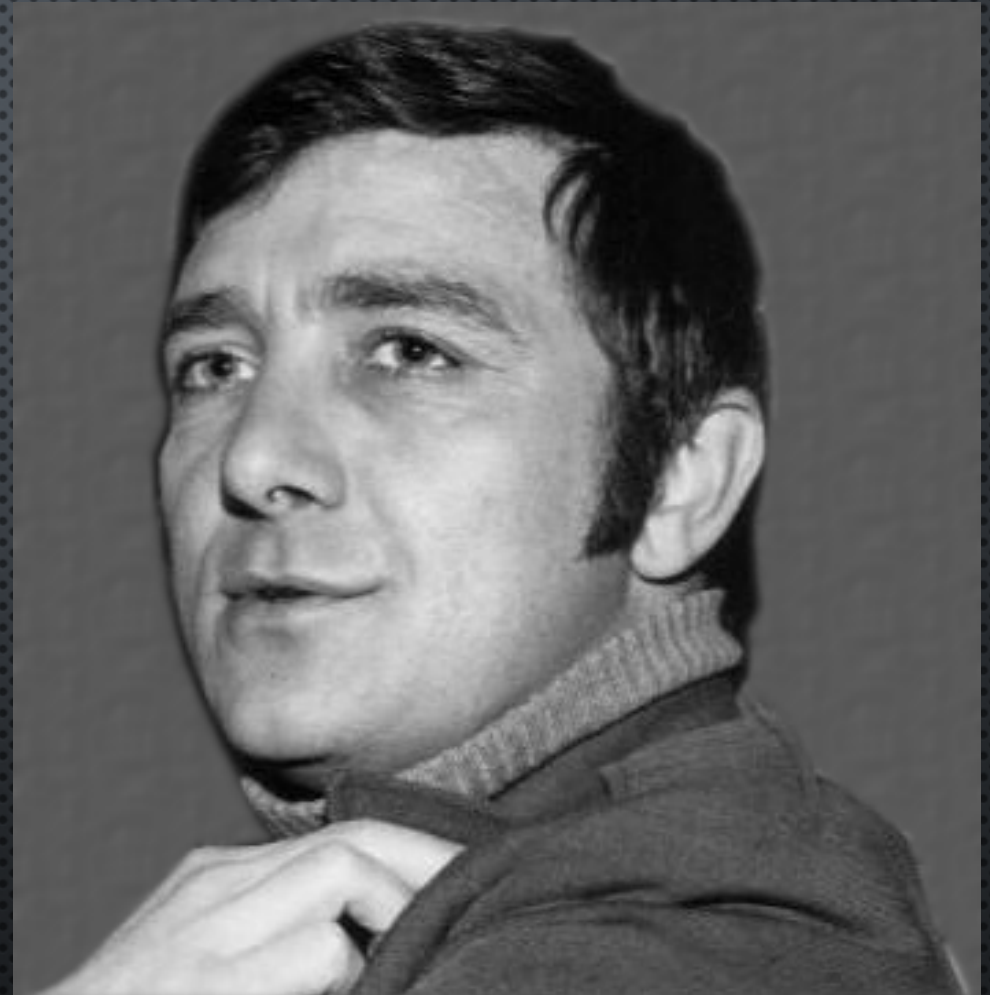
5

10



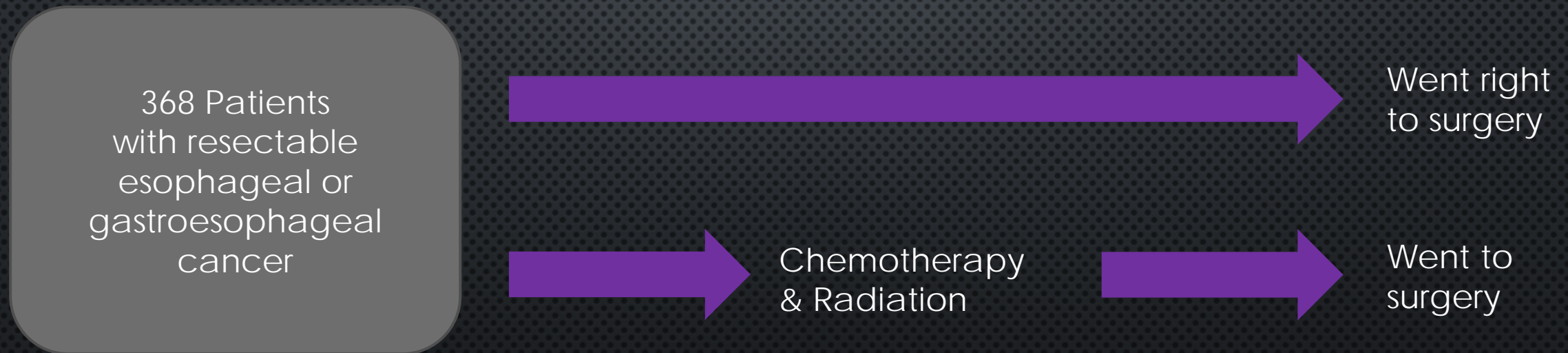
# RICHARD

- DIAGNOSED WITH SQUAMOUS CELL CARCINOMA OF THE MID-ESOPHAGUS
- PET SHOWED UPTAKE AT MID-ESOPHAGUS ONLY
- THORACIC SURGEON AGREES TO OPERATE





# THE CROSS CLINICAL TRIAL



NEJM 2012; 366:2074-2084

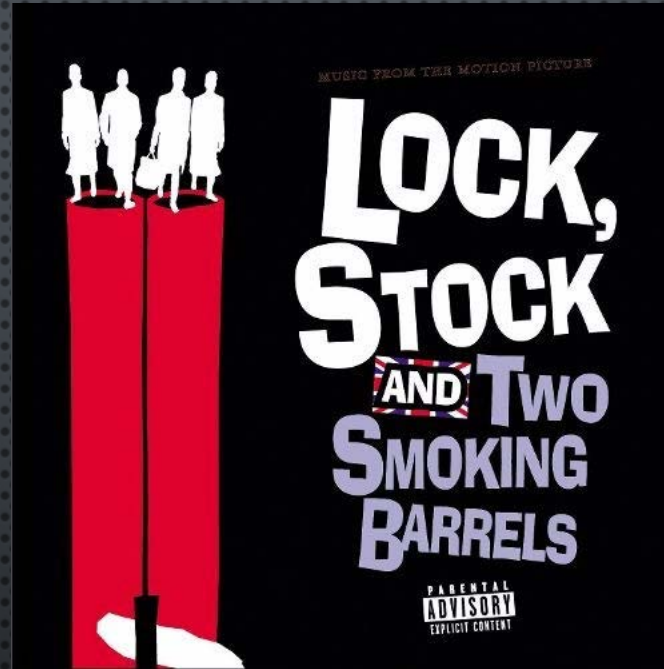


The diagram shows a timeline for the 8-week group. It features a series of red vertical bars representing Carboplatin/paclitaxel treatment, spaced out over time. Between these red bars are groups of gray vertical bars representing Radiation treatment. A legend indicates that red bars correspond to Carboplatin/paclitaxel and gray bars correspond to Radiation treatment. A blue vertical bar on the right is labeled 'Resection'. The text '8 weeks later' is positioned below the timeline.



8 weeks later

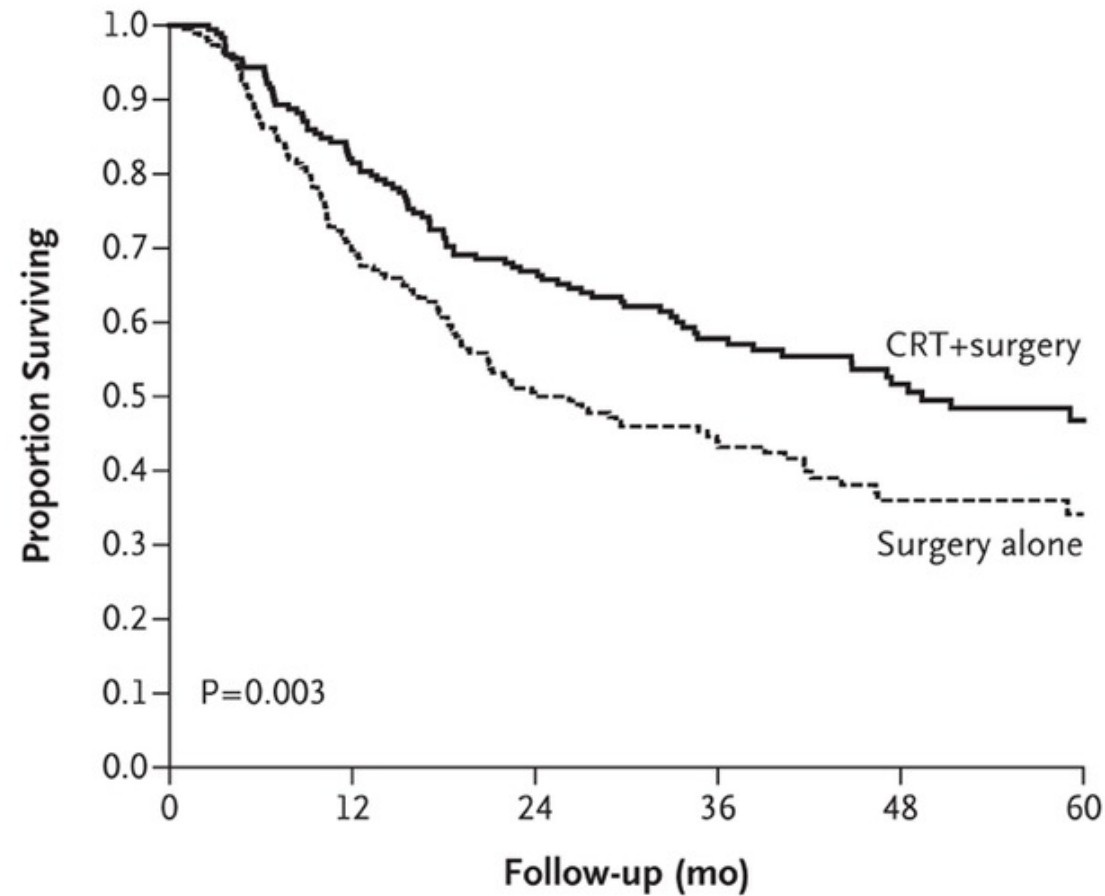




Chemotherapy + Radiation = Dual Modality Treatment  
(ChemoRadiation + Surgery = Tri-Modality Treatment)



### A Survival According to Treatment Group



~50% alive  
at 5 years

~40% alive  
at 5 years

#### No. at Risk

CRT+surgery	178	145	119	75	49	28
Surgery alone	188	131	94	62	33	17
Total	366	276	213	137	82	45



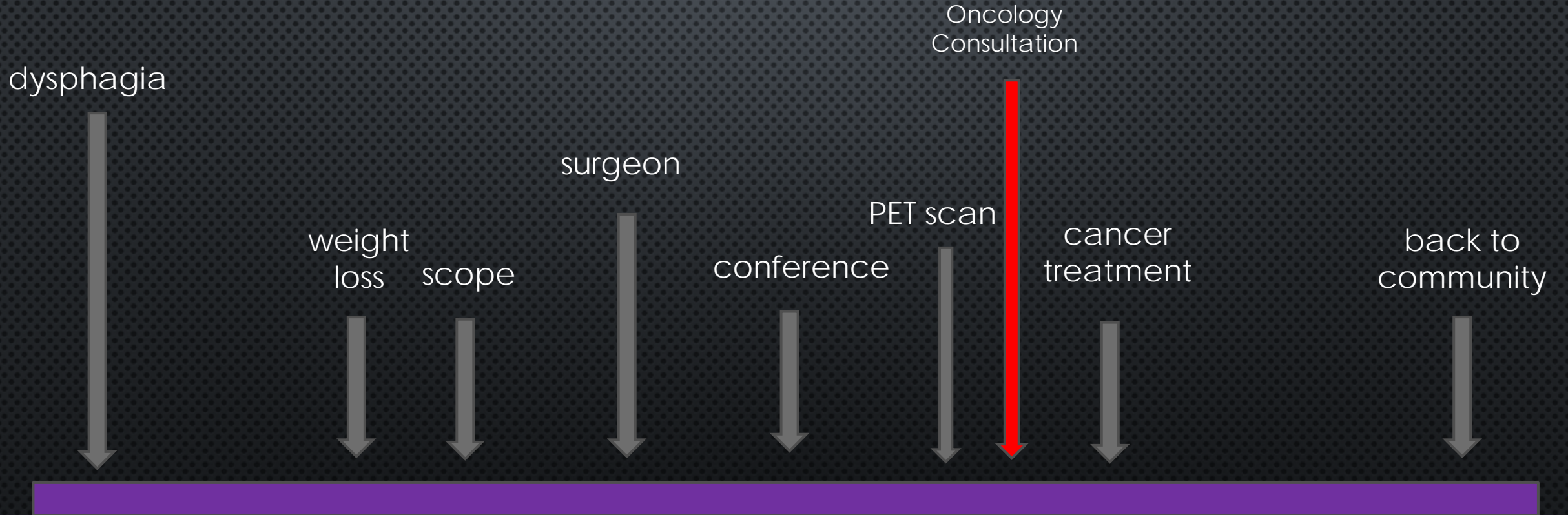
# ANOTHER QUESTION...

WOULD YOU BE DISAPPOINTED WITH THESE NUMBERS?

- **YES**
- **NO**



# RICHARD'S TIMELINE

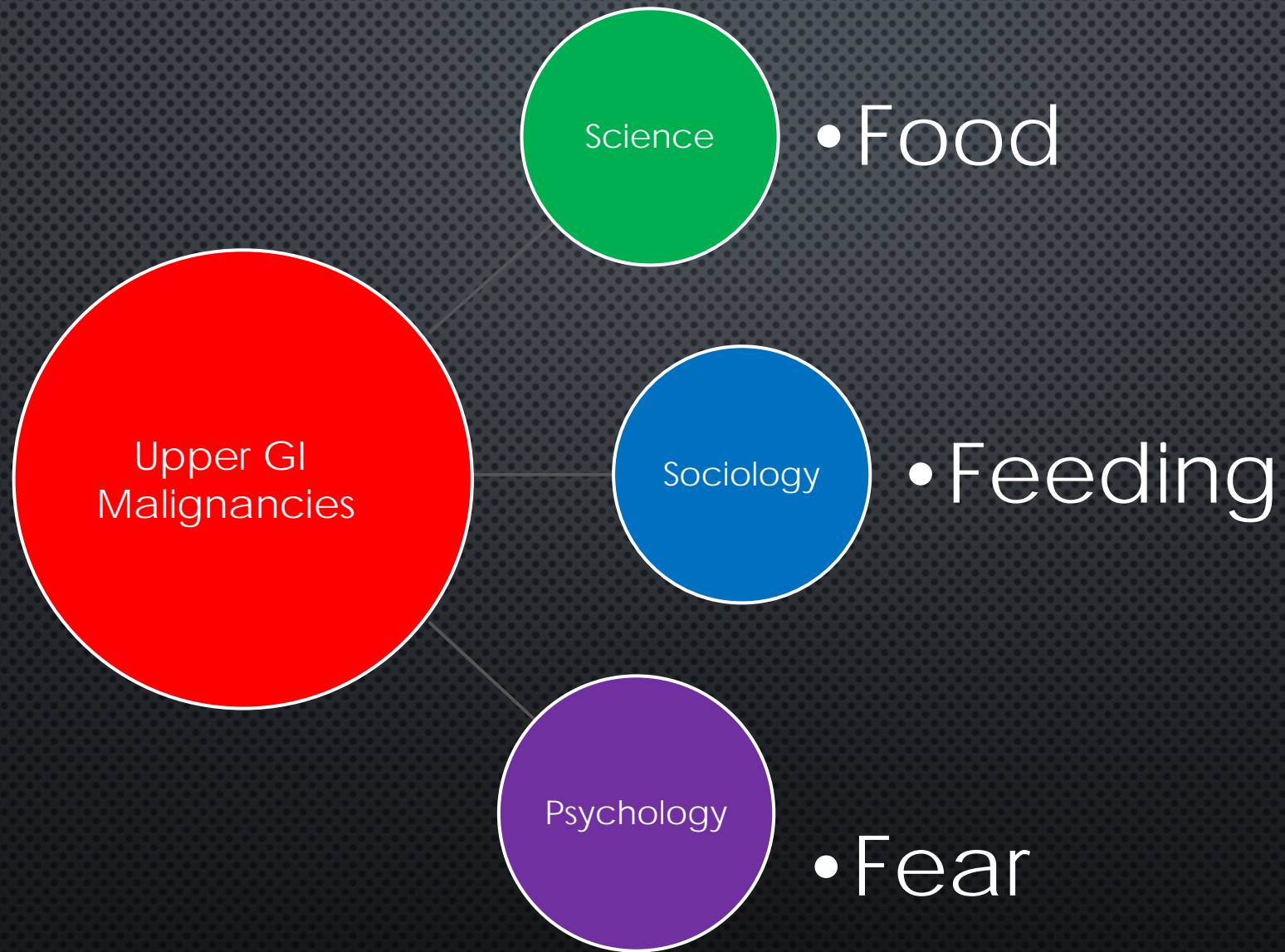




## 7. Follow Up

- Patients who have undergone treatment for superficial disease should have endoscopic surveillance.
- Patients who had radiation or surgery are at risk of developing esophageal strictures resulting in dysphagia which can be treated with dilation or stenting. There is no evidence that routine imaging or laboratory investigations are useful in detecting recurrences or metastases at a stage where interventions are curative. **Early detection of asymptomatic metastases does not enhance survival.**
- Investigations should be performed based the clinical presentation of a patient who is suspected of having recurrent or metastatic disease.







# THE SCIENCE

## SQUAMOUS CELL CARCINOMA

- RELATED TO SMOKING
- RELATED TO DRINKING
- DIET/REGIONAL RISK FACTORS

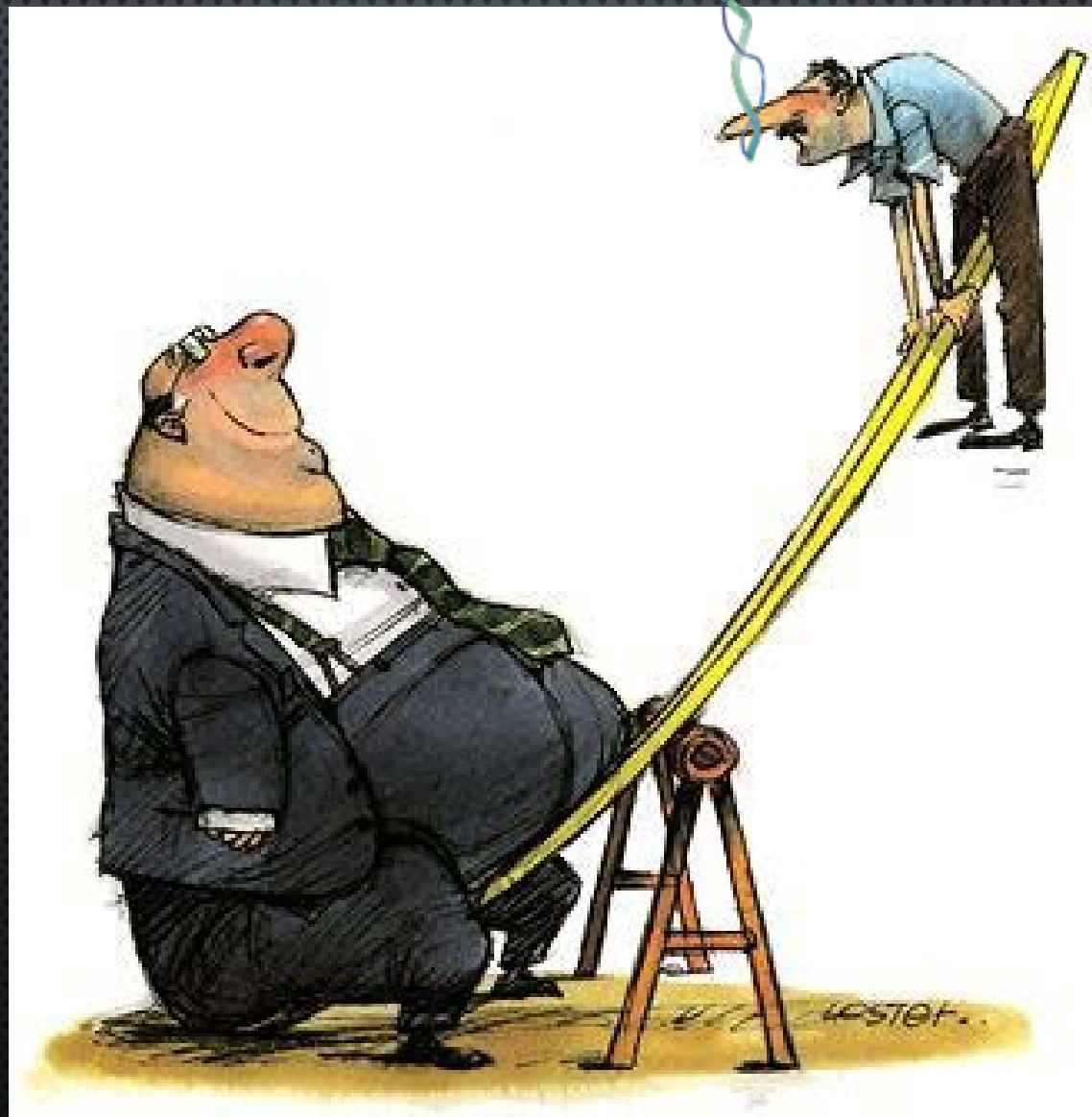
## ADENOCARCINOMA

- CAUSED BY REFLUX (RELATED TO OBESITY)
- WATCH THE QUANTITY OF INTAKE
- WATCH THE CONTENT OF INTAKE



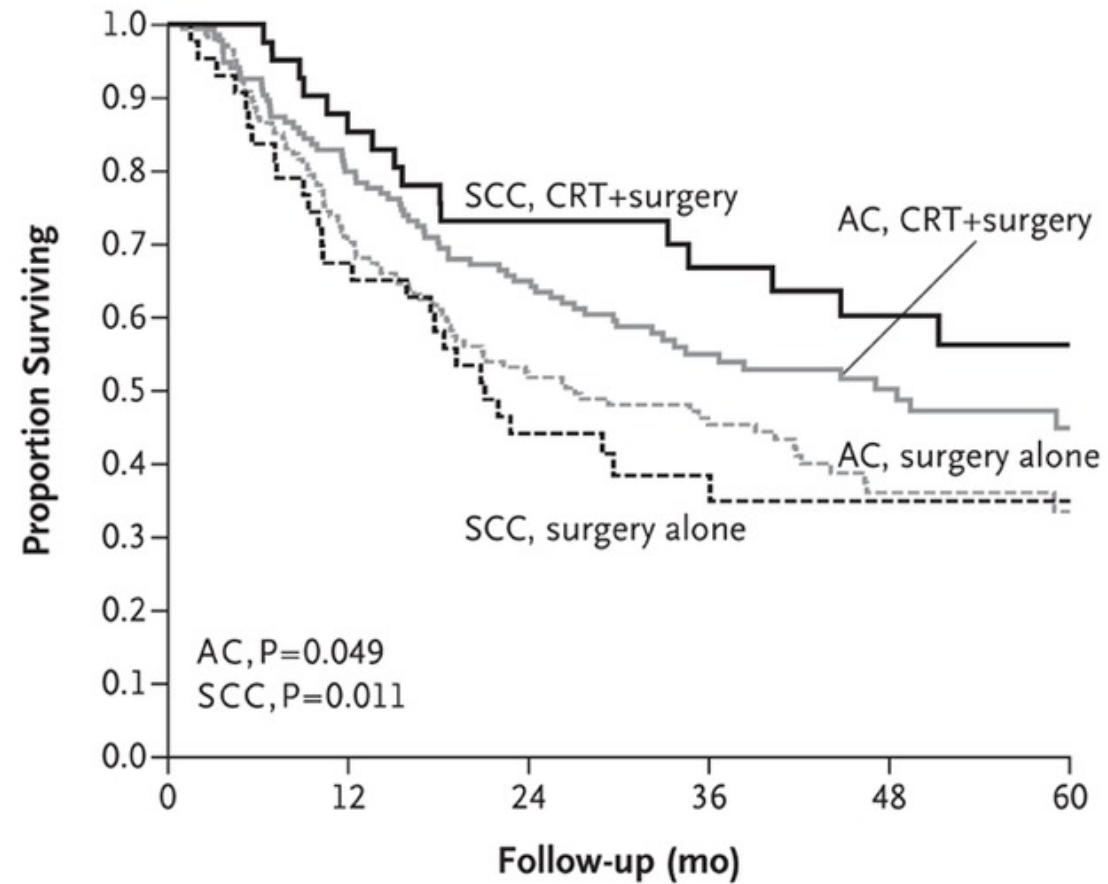
Science

## Shift to Adenocarcinoma from Squamous Cell Carcinoma





## B Survival According to Tumor Type and Treatment Group



### No. at Risk

AC, CRT+surgery	134	107	87	53	34	18
AC, surgery alone	141	99	73	50	25	10
SCC, CRT+surgery	41	35	30	21	15	8
SCC, surgery alone	43	29	19	11	8	4
Total	359	270	209	135	82	40



# THE SOCIOLOGY

## RICHARD'S LOVED ONES

- NO MORE THANKSGIVING DINNER...
- NO MORE DINNER FOR TWO...
- NO MORE DINNERS OUT WITH FRIENDS...

## RICHARD

- "SEES CERTAIN FOODS AS THE ENEMY"\*
- CAN'T GAIN WEIGHT AND DOESN'T LIKE TO BE FUSSED OVER...

\*Due to dumping syndrome



# THE PSYCHOLOGY

- UPPER GI SYMPTOMS ARE COMMON, UPPER GI CANCERS ARE NOT
- DYSPHAGIA MAKES US POOR HISTORIANS
- DESPITE A RIGOROUS WORK-UP AND AGGRESSIVE THERAPY, THERE IS NO SPECIFIC FOLLOW UP FOR RICHARD...
- “NEVER THE SAME SINCE TREATMENT”



# GASTRIC CANCER

- FRED CAME TO SEE ME IN 2018...





# GASTRIC CANCER STORYLINE



- YEARS OF MILD ABDOMINAL PAIN
- EVENTUALLY LED TO (ALARMING) WEIGHT LOSS
- FOUND ANEMIC IN THE WORK UP
- SEEN BY SURGEON WHO REQUESTED SYSTEMIC THERAPY



# OUR PLAN-A...

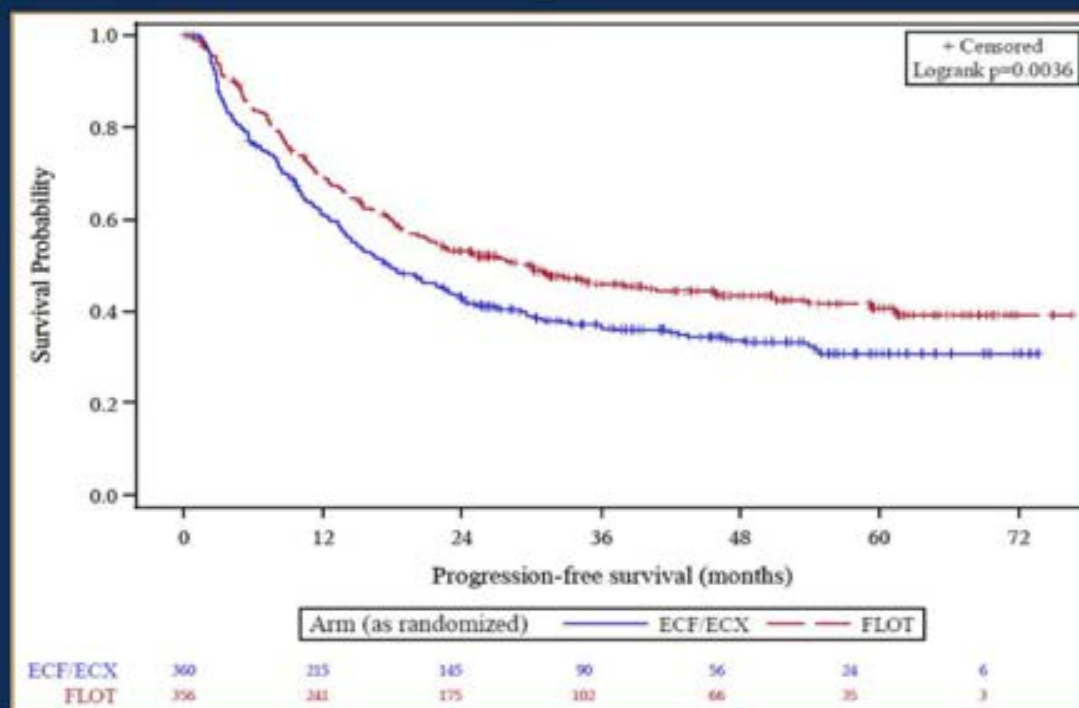
## FLOT Regimen

- **T** docetaxel d1 50 mg/m<sup>2</sup> iv inf.
- **O** oxaliplatin d1 85 mg/m<sup>2</sup> iv inf.
- **L** leucovorin d1 200 mg/m<sup>2</sup> iv inf.
- **F** 5-FU d1 2.600 mg/m<sup>2</sup> iv 24h inf.
  - repeated every 2 weeks

- PROVIDE A PERIOPERATIVE CHEMO SANDWICH
- TOXIC REGIMEN BUT PROVIDES BEST RESULTS WE'VE SEEN IN THE CURATIVE SETTING



# FLOT4: Progression-Free Survival



	ECF/ECX	FLOT
mPFS 18 months		30
	[15-22]	[21-41]

HR 0.75 [0.62-0.91]  
p=0.004 (log rank)

PFS rate*	ECF/ECX	FLOT
2y		43%
		53%
3y		37%
		46%
Projected PFS rates		31%
		41%

PRESENTED AT: ASCO ANNUAL MEETING '17 | #ASCO17

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Presented by: Salah-Eddin Al-Batran



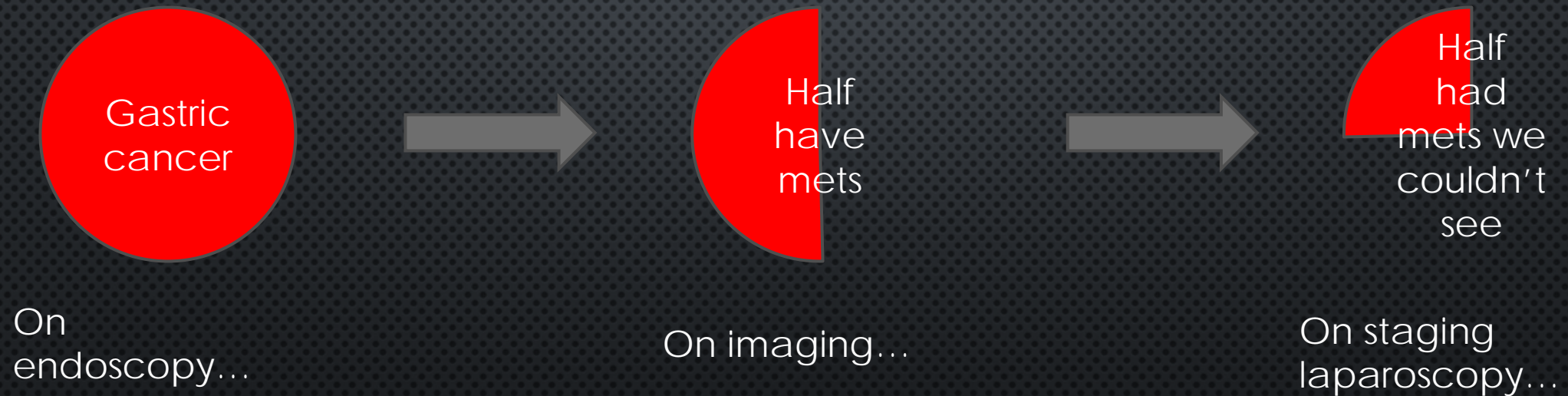
# HEMOGLOBIN 51!



- ANEMIA BECAME SEVERE
- CONSIDERED RADIATION
- MULTIDISCIPLINARY CONFERENCE SUGGESTS GOING STRAIGHT TO SURGERY



# BACK TO SURGEON FOR STAGING LAPAROSCOPY...THEN SURGERY





# ADVANCED GASTRIC CANCER



- PROGNOSIS POOR
- LIFE EXPECTANCY < 1 YEAR
- CONSIDERING PALLIATIVE SYSTEMIC THERAPY



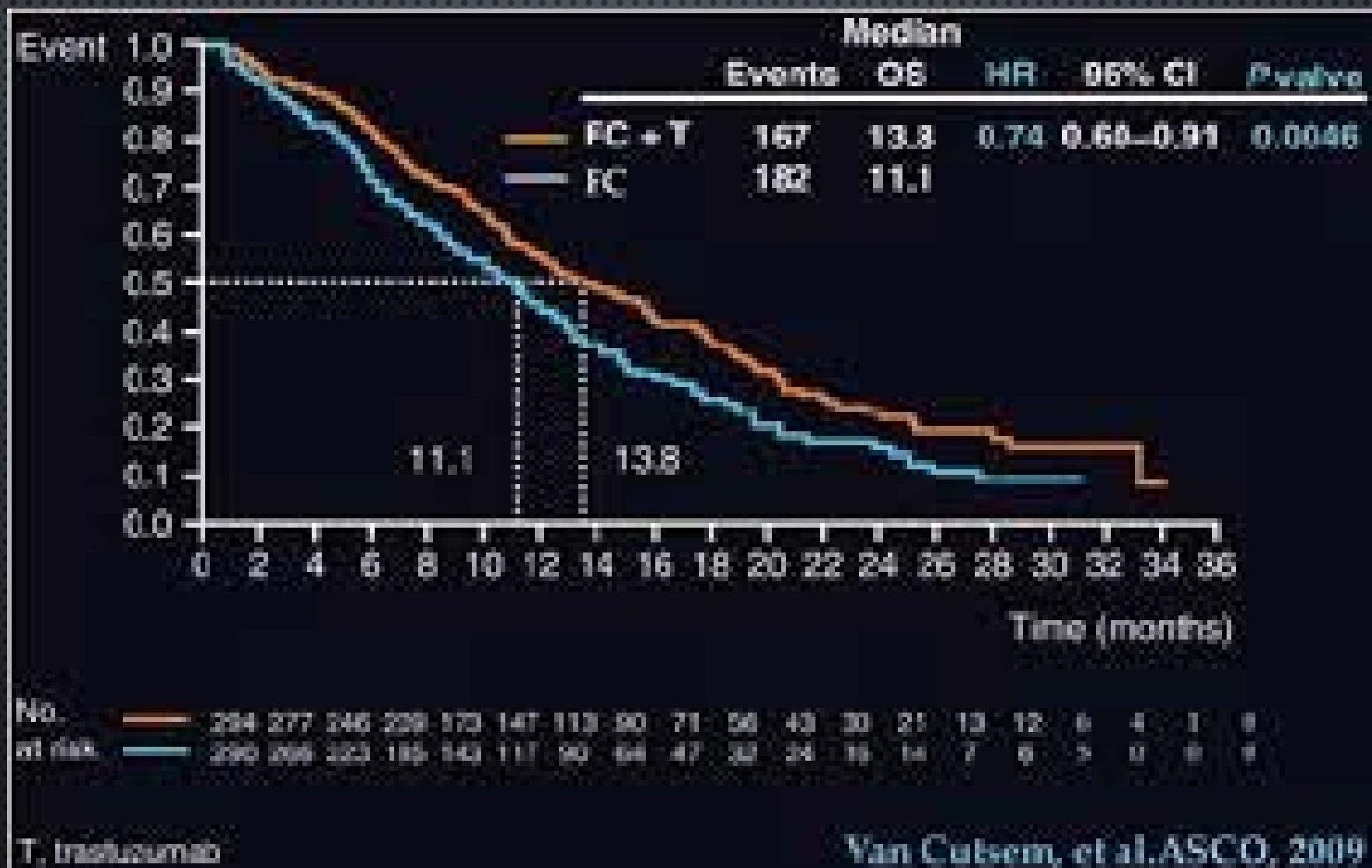
# THE TOGA TRIAL...

- SOME GASTRIC CANCERS OVEREXPRESS THE HER-2 PROTEIN
- CHEMO + TRASTUZUMAB (HERCEPTIN) MAY EXTEND SURVIVAL



Peter O-Toole on twitter







# OUR PATIENTS ARE STARS...



- ADVANCED DISEASE (ACCEPTS DIAGNOSIS)
- GOAL #1 IS MAINTAIN QUALITY OF LIFE
- GOAL #2 IS TO PROLONG SURVIVAL

Photo from the DailyMail.uk



# FOLLOW UP



## BY THE BOOK...

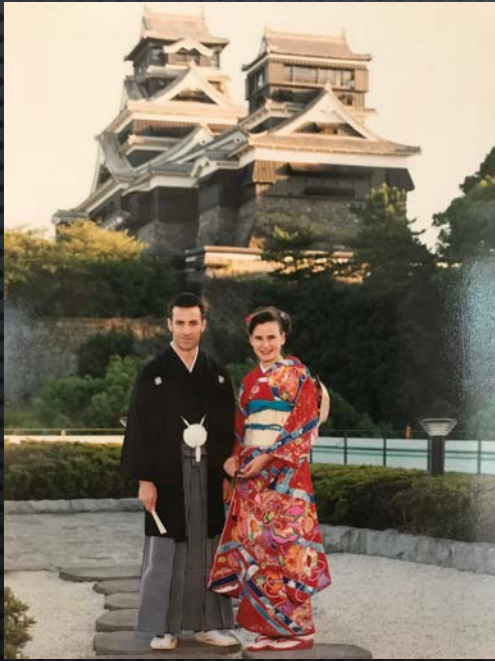
- NO TESTS REQUIRED
- WORK UP SYMPTOMS OR SIGNS OF RECURRENCE

## IN MY CLINIC...

- WHAT IS IMPORTANT TO YOU?
- HOW DO YOU WANT TO PROCEED?
- SET REASONABLE LIMITS



## TO JAPAN...



- HIGH RATES DUE TO HIGH SALT INTAKE, HIGH RATES OF SMOKING AND HELICOBACTER PYLORI INFECTION
- SCREENING WORKS IN JAPAN
- ERADICATION OF H.PYLORI IS A NATIONAL GOAL



Science

# SCREEN HOUSEHOLD FOR *HELICOBACTER PYLORI*





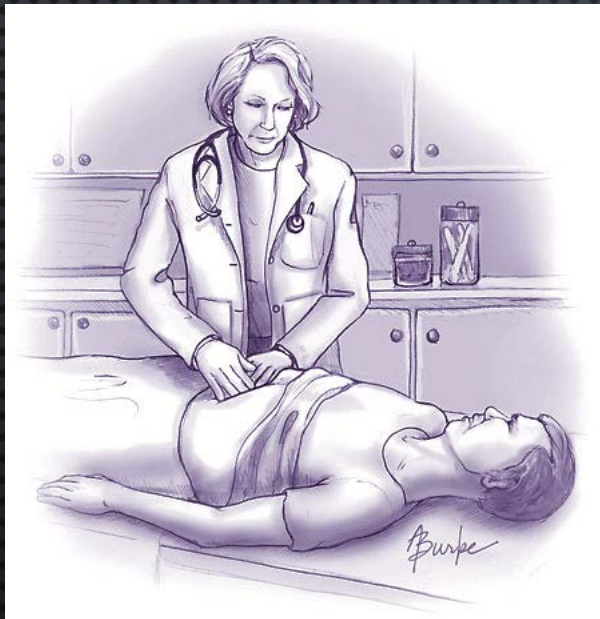
# THE SOCIOLOGY OF STARVING



- FAMILY STRUGGLES WITH HIS WEIGHT LOSS, ANOREXIA
- DISCUSSED CONCEPT OF “STARVING TO DEATH”



# GI SYMPTOMS



- DIFFICULT TO REASSURE FAMILY MEMBERS WHO WILL HAVE ABDOMINAL PAIN IN FUTURE



CONTINUING DOWN THE PIPE...



# BOWEL CANCER

## SMALL BOWEL

- 6 METRES
- RARE TO FIND CANCER
- NO EVIDENCE
- POOR PROGNOSIS
- TREATMENTS DON'T WORK

## LARGE BOWEL

- 1 METRE
- COMMON TO FIND CANCER
- ABUNDANT EVIDENCE
- GOOD PROGNOSIS
- TREATMENTS "WORK"



# SMALL BOWEL CANCER

- CHARLIE CAME TO SEE ME AS A SECOND OPINION IN 2012...





# CHARLIE'S QUESTIONS

- WHY DID I GET THIS DISEASE?
- WHY DID MY ONCOLOGIST TELL ME "THERE WAS NOTHING TO DO?"
- WHAT ARE MY "CHANCES"?





# LET'S TALK ABOUT CHARLIE...

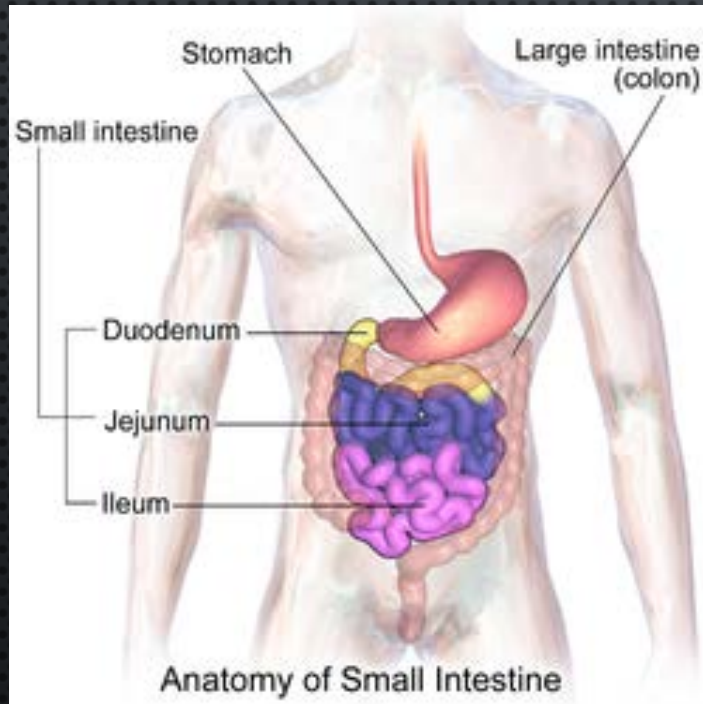


Charles M. Schulz  
(photo from Wikipedia)

- 60-70 YEARS OLD, HEALTHY, MALE
- SMOKED/DRANK (A BIT)
- NO EVIDENCE OF HEREDITARY DISEASE



# CANCER IN THE SMALL BOWEL?



- 800 CANADIANS DIAGNOSED WITH SMALL BOWEL CANCER ANNUALLY, BUT OVER 25 000 DIAGNOSED WITH COLON CANCER
- SMALL SERIES TELL US THAT ADJUVANT CHEMOTHERAPY IS NOT EFFECTIVE
- DIFFICULT TO MAKE CONCLUSIONS WITH SUCH LIMITED DATA
- CAN WE REALLY EXTRAPOLATE FROM COLON LITERATURE?



WOULD YOU PURSUE  
ADJUVANT CHEMOTHERAPY IN THIS SETTING?

- YES
- NO



# COMPLETED FOLFOX...

- USED COLON CANCER GUIDELINES TO DESCRIBE FOLLOW UP / SURVEILLANCE...



# SMALL BOWEL CANCER



- CHARLIE CAME BACK TO SEE ME IN 2015...



# METASTATIC/RECURRENT DISEASE OF THE SMALL BOWEL



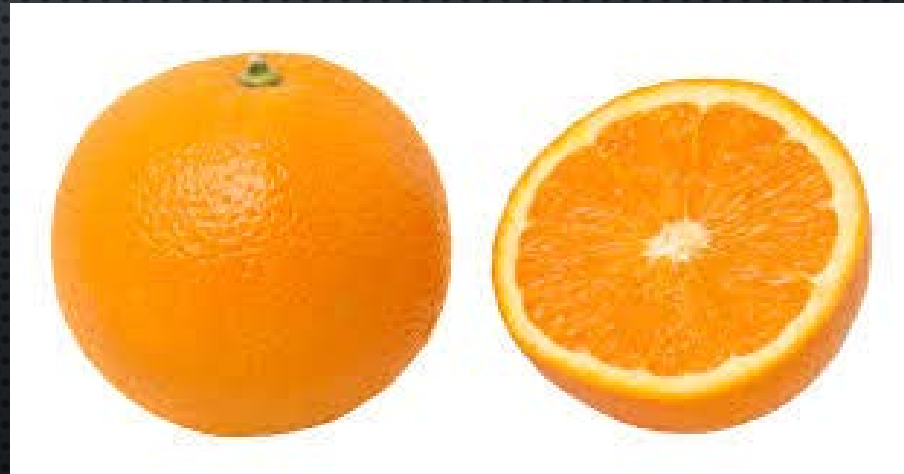


# METASTATIC/RECURRENT DISEASE OF THE SMALL BOWEL

LARGE BOWEL (COLON)



SMALL BOWEL





# METASTATIC SMALL BOWEL CANCER



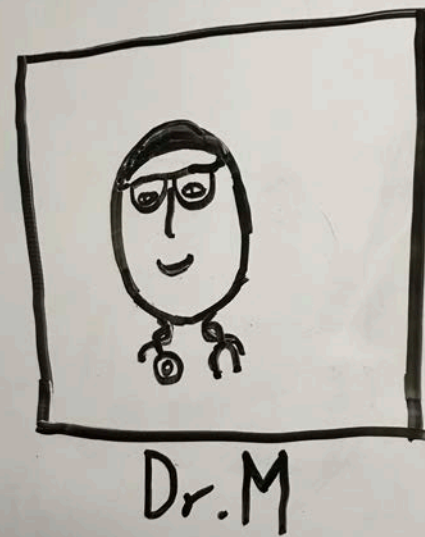


# WOULD YOU PURSUE PALLIATIVE SYSTEMIC THERAPY?

- YES, FOR ME
- YES, FOR OTHERS
- NO



- LET'S RECAP!





## ALARM SYMPTOMS.

- DIFFICULT TO DETECT (DYSPHAGIA)
- OFTEN AREN'T ALARMING SYMPTOMS UNTIL TOO LATE (WEIGHT LOSS)

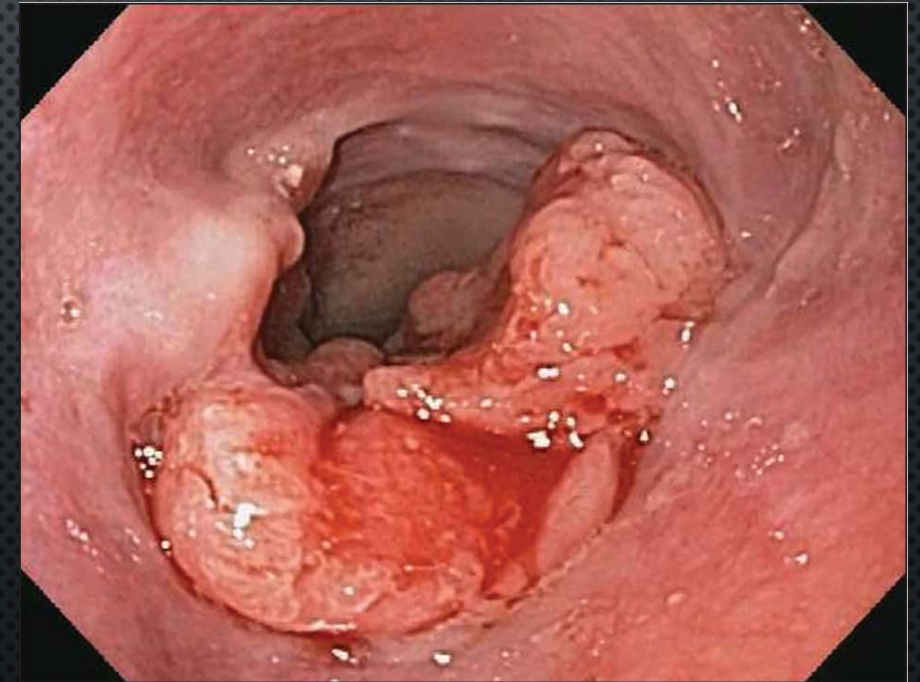
## FOLLOW UP.

- ENDOSCOPY CAN BE HELPFUL
- NOTHING ELSE "WORKS" (AS PER LITERATURE)
- BUT USE CT, BLOOD TESTS IF THERE ARE SYMPTOMS OR SIGNS



# RECAP: ESOPHAGEAL CANCER

- THERE ARE TWO FLAVOURS OF ESOPHAGEAL CANCER
- SHIFTING FROM SQUAMOUS CELL CARCINOMA TO ADENOCARCINOMA

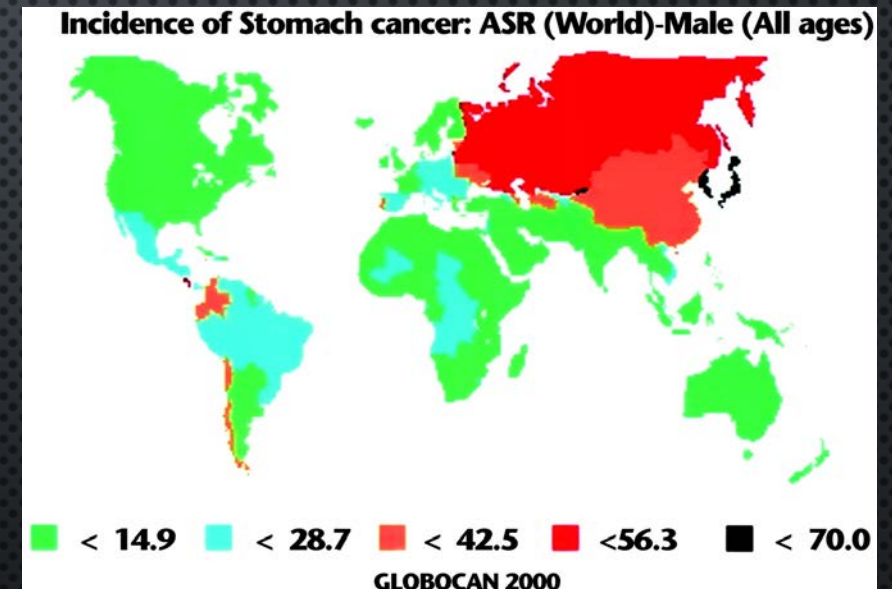


From aafp.org



# RECAP: GASTRIC AND ESOPHAGEAL CANCER

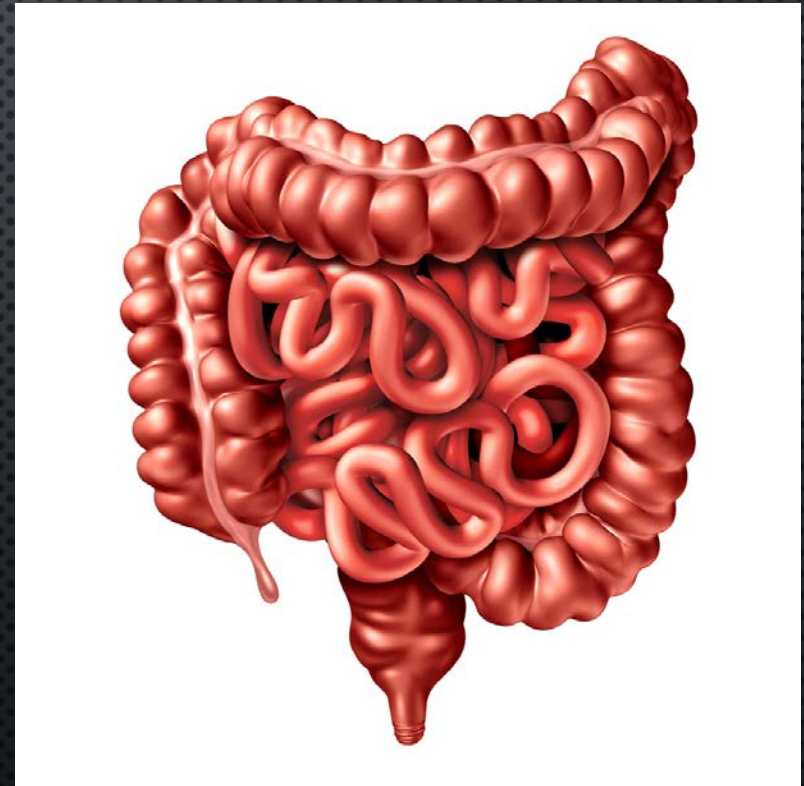
- HUGE ISSUE WORLDWIDE; KNOW WHERE YOUR PATIENTS ARE FROM
- TREATMENT FOR CURE CAN BE VERY CHALLENGING
- PALLIATIVE TREATMENTS OFTEN PROVIDE SUBOPTIMAL RESULTS





# RECAP: SMALL BOWEL CANCER

- SMALL BOWEL CANCER IS RARE
- TREATMENT APPROACHES BORROW FROM THE COLON LITERATURE
- TREATMENT RESULTS ARE FAR FROM WHAT WE SEE WITH COLON CANCER





# RECAP: THE COMPLEXITY OF UPPER GI MALIGNANCIES

- FOOD: EAT REAL FOOD!
- FEEDING: EATING IS WHAT WE DO
- FEAR: DEEP ANXIETY BEHIND GI SYMPTOMS CAN'T BE ALLEVIATED BY TESTS





THANK YOU!

...be the person your dog thinks you are...

