GI Case Studies

David Rakel, MD

Professor & Chair

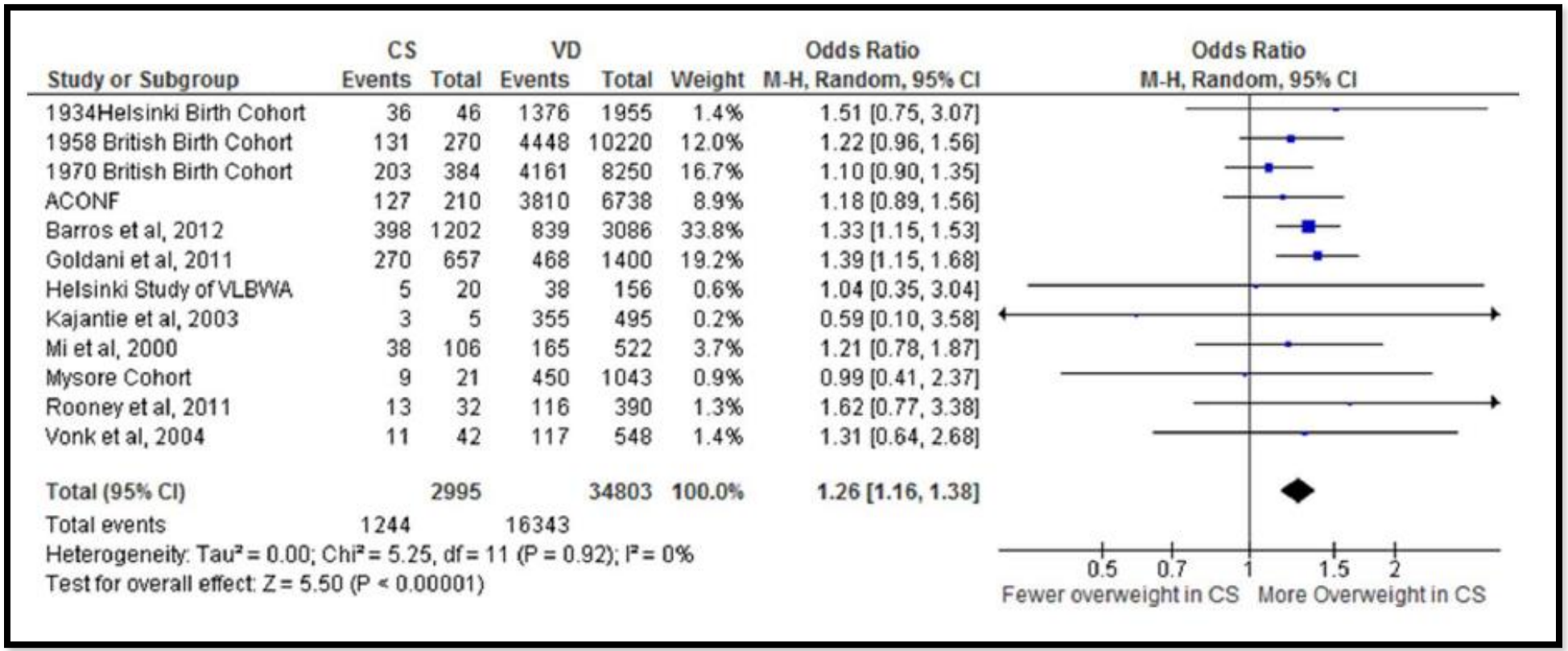
UNM Dept. of Family & Community Medicine

SCHOOL OF MEDICINE

First Exposure

- Birth (C/S vs Vagina)
- Feeding (Bottle vs Breast)
- Group B Strep Prophylaxis? (Antibiotic Exposure)

C/S and risk of obesity

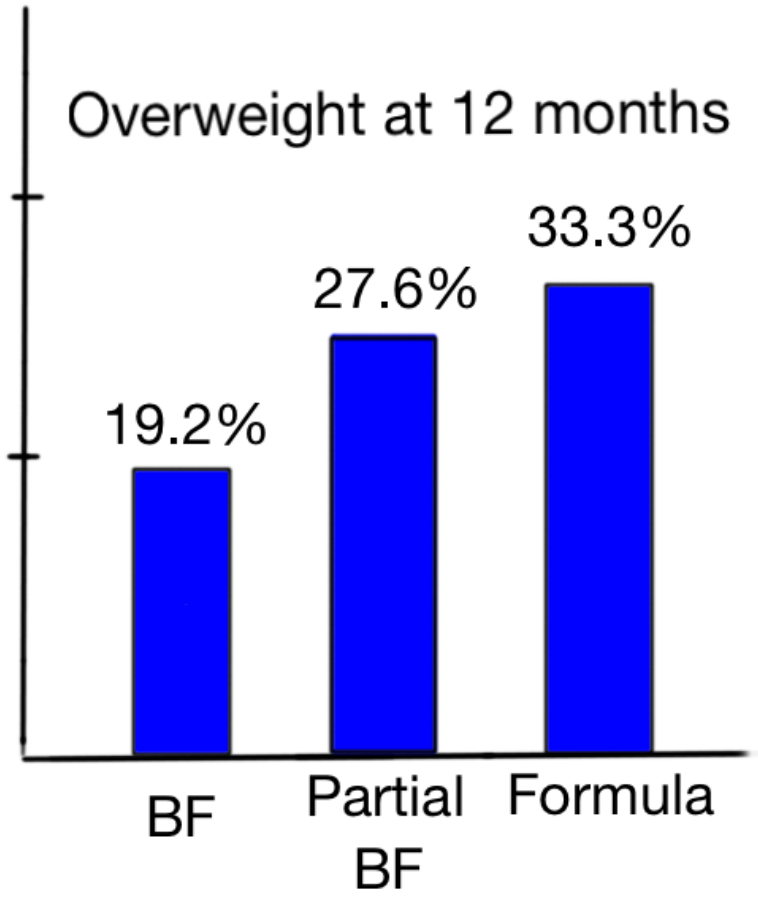


Study or Subgroup	CS Events	CS Total	VD Events	VD Total	Weight	Odds Ratio M-H, Random, 95% CI
1934Helsinki Birth Cohort	36	46	1376	1955	1.4%	1.51 [0.75, 3.07]
1958 British Birth Cohort	131	270	4448	10220	12.0%	1.22 [0.96, 1.56]
1970 British Birth Cohort	203	384	4161	8250	16.7%	1.10 [0.90, 1.35]
ACONF	127	210	3810	6738	8.9%	1.18 [0.89, 1.56]
Barros et al, 2012	398	1202	839	3086	33.8%	1.33 [1.15, 1.53]
Goldani et al, 2011	270	657	468	1400	19.2%	1.39 [1.15, 1.68]
Helsinki Study of VLBWA	5	20	38	156	0.6%	1.04 [0.35, 3.04]
Kajantie et al, 2003	3	5	355	495	0.2%	0.59 [0.10, 3.58]
Mi et al, 2000	38	106	165	522	3.7%	1.21 [0.78, 1.87]
Mysore Cohort	9	21	450	1043	0.9%	0.99 [0.41, 2.37]
Rooney et al, 2011	13	32	116	390	1.3%	1.62 [0.77, 3.38]
Vonk et al, 2004	11	42	117	548	1.4%	1.31 [0.64, 2.68]
Total (95% CI)		**2995**		**34803**	**100.0%**	**1.26 [1.16, 1.38]**
Total events	1244		16343			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 5.25$, $df = 11$ ($P = 0.92$); $I^2 = 0\%$

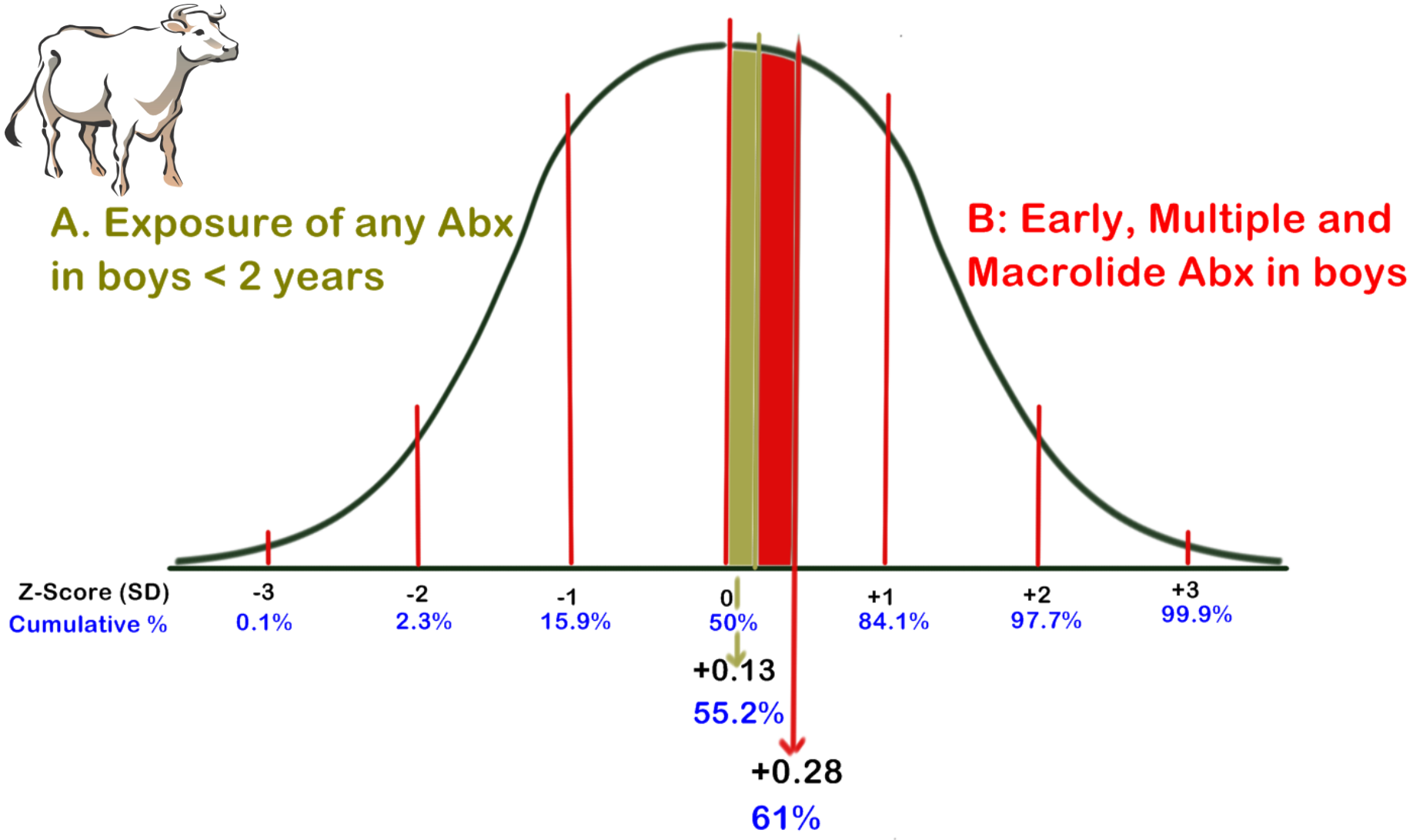
Test for overall effect: $Z = 5.50$ ($P < 0.00001$)

Darmasseelane, K., et al., *Mode of delivery and offspring body mass index, overweight and obesity in adult life: a systematic review and meta-analysis.* PLoS One, 2014. **9**(2)



Any Formula = ↑ obesity risk at 12 mths and changes the microbiome

Forbes JD, et al. Association of Exposure to Formula in the Hospital and Subsequent Infant Feeding Practices with Gut Microbiota and Risk of Overweight in the First Year of Life. JAMA Pediatrics. June 4th, 2018.



Saari, A., et al., *Antibiotic exposure in infancy and risk of being overweight in the first 24 months of life.* Pediatrics, 2015. **135**(4): p. 617-26.

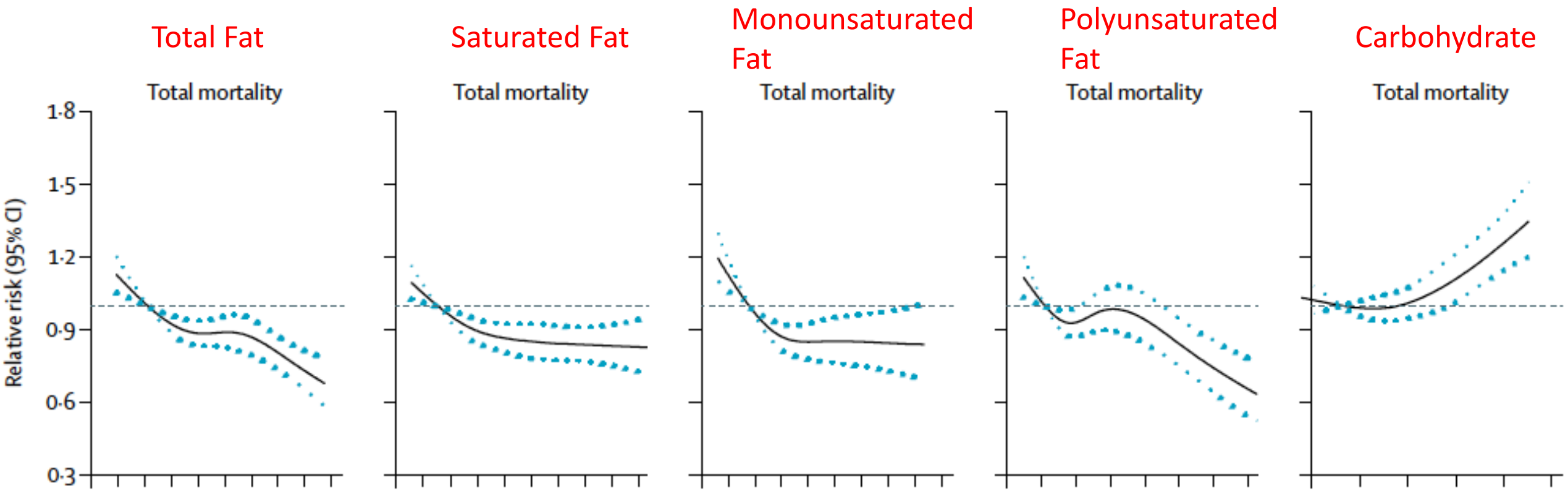
Margarete, R1

28 yo female UNM Internal Medicine resident who is a vegetarian but eats mainly processed carbs that she eats on the run when she has time to grab something. She suffers from bloating, gas and cramping. She reports stress associated with residency and trying to maintain a personal relationship. She uses a PPI occasionally without significant benefit.

Handout Tools

- Elimination Diet
- FODMaPs
- Intestinal Permeability (”Leaky Gut”)
- How to taper off a PPI
- Gut directed hypnotherapy (Balloon Technique)
- Breathing Exercises (Vagal Nerve Stimulation)

The PURE Study: Mortality Rates for % energy from each food group



Dehghan M, Mente A, Zhang X, et al. Associations of fats and carbohydrate intake with cardiovascular disease and mortality in 18 countries from five continents (PURE): a prospective cohort study. *Lancet.* 2017.

Nutrition Facts

Serving Size 2/3 cup (55g)
Servings Per Container About 8

Amount Per Serving

Calories 230 Calories from Fat 72

	% Daily Value*
Total Fat 8g	**12%**
Saturated Fat 1g	**5%**
Trans Fat 0g	
Cholesterol 0mg	**0%**
Sodium 160mg	**7%**
Total Carbohydrate 37g	**12%**
Dietary Fiber 4g	**16%**
Sugars 1g	
Protein 3g	
Vitamin A	10%
Vitamin C	8%

Nutrition Facts

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Cholesterol 0mg	**0%**
Sodium 160mg	**7%**
Total Carbohydrate 37g	**13%**
Dietary Fiber 4g	**14%**
Total Sugars 12g	
Includes 10g Added Sugars	**20%**
Protein 3g	

Sweetness > Sugar

Aspartame = 200x Sweeter

Saccharin = 500x Sweeter

Sucralose = 600x Sweeter

Advantame = 20,000x Sweeter

Sylvetsky AC, Rother KI. Nonnutritive Sweeteners in Weight Management and Chronic Disease: A Review. Obesity. 26, 635-640.2018.

The 3 Faces of Wheat

1. Celiac: Autoimmune
2. Protein Sensitivity, NCGS
3. Fructans: Sugar, FODMaPs

FODMaP Diet (IBS)

Fermentable-Oligosaccharides

Wheat, Rye (onion, garlic, leeks)

Disaccharides

Milk products

Monosaccharides

Fructose (apples, pears), HFCS, Honey

Polyols

Sugar alcohols: sorbitol, xylitol, mannitol, maltitol

Good symptom relief in 75%, No effect in 25%.

Jl of Gastroenterology and Hepatology ***25*** *(2010) 252–258*

Modified FODMaP: Start Simple

- Reduce anything made from bleached white flower (Fermentable Oligosaccharides)
- Reduce dairy (lactulose…. Disaccharides)
- Reduce sugar in general (fructose corn syrup, simple sugars…. Monosacharides)
- Reduce Polyol sugars…. Any artificial sweetener that ends with “-ol”

Low FODMaP App

View in iTunes

This app is designed for both iPhone and iPad

$7.99

Category: Medical
Updated: Apr 16, 2015
Version: 1.4
Size: 184 MB
Language: English
Seller: Monash University
© 2012 Monash University
Rated 12+ for the following:
Infrequent/Mild Medical/Treatment Information

Compatibility: Requires iOS 7.0 or later. Compatible with iPhone, iPad, and iPod touch. This app is optimized for iPhone 5, iPhone 6, and iPhone 6 Plus.

Description

Researchers at Monash University have developed a diet and corresponding app to assist in management of the gastrointestinal symptoms associated with Irritable Bowel Syndrome (IBS). The Monash University Low FODMAP diet works by restricting foods high in some carbohydrates called FODMAPs.

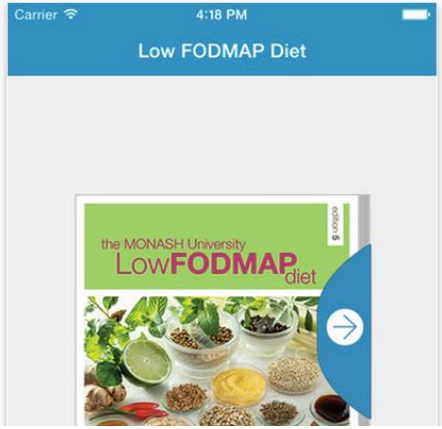
The Monash University Low FODMAP Diet Support ...More

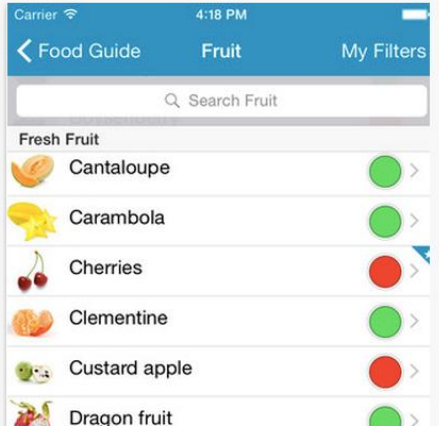
What's New in Version 1.4

- Added new Monash University Low FODMAP Certified Foods to Guide

Screenshots

iPhone | iPad





Treatment (Margarete)

- MBCT with Gut Directed Hypnotherapy
- More high fiber multi-colored whole foods, less fat and sugar.
- FODMaPs
- Probiotic x 4 weeks (Lacto, Bifido & Saccharomyces) w/ soluble fiber.
- Encourage a mental health day

Joe, Store Manager

A 32 yo Auto-Supply Store manager who reports periodic constipation and worsening atopic dermatitis. HLA DQ2/DQ8 is negative and tTG IgA negative, DGP = deaminated gliadan peptide antibody negative. He has taken oral prednisone for severe flares of his eczema and required prolonged course of antibiotics for an infection he picked up in Iraq when he was in the service. He eats a typical American Diet with plenty of ‘white’ foods, meat and potatoes. He also takes omeprazole 40 mg daily for GERD.

Handout Tools

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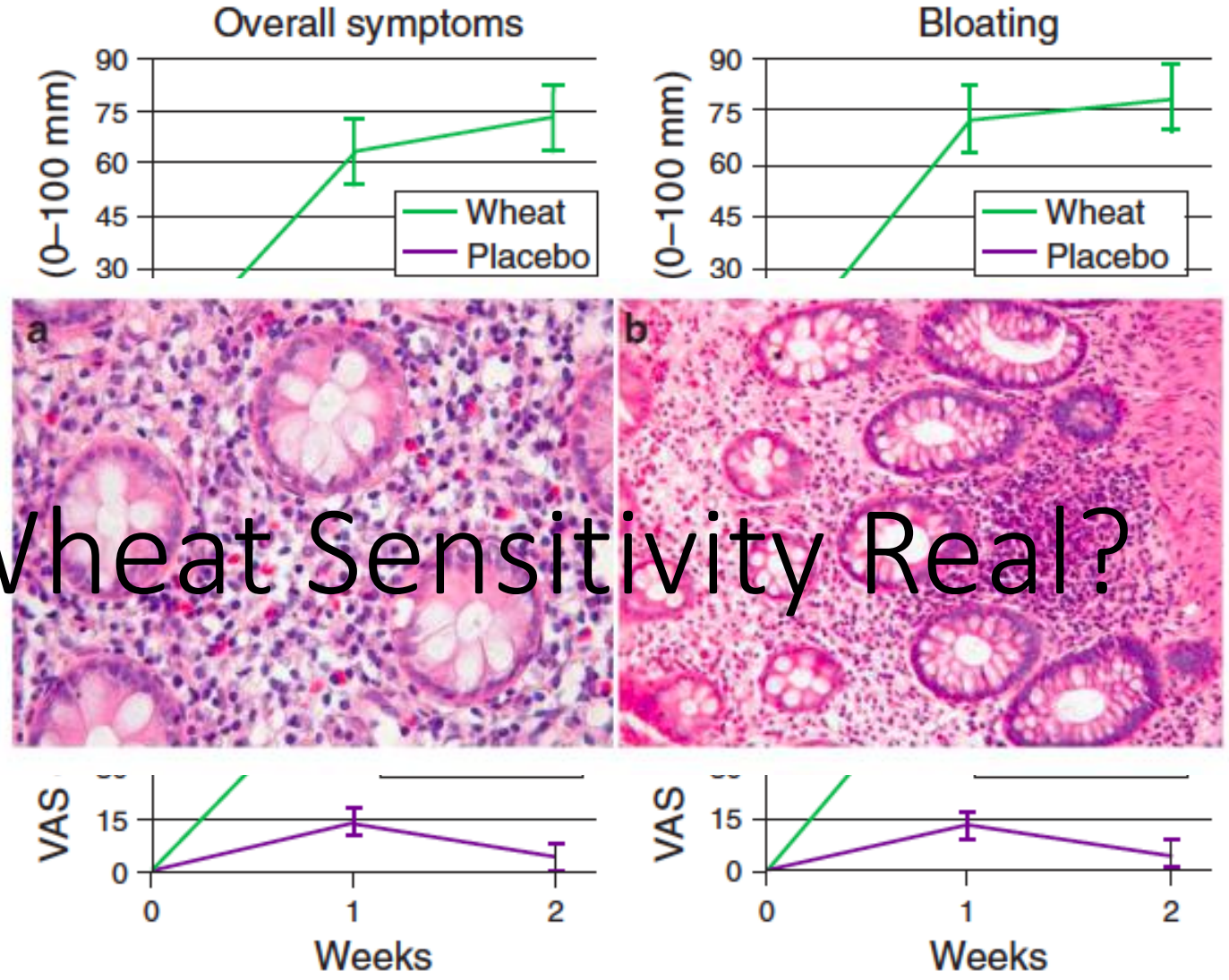
Is Wheat Sensitivity Real?



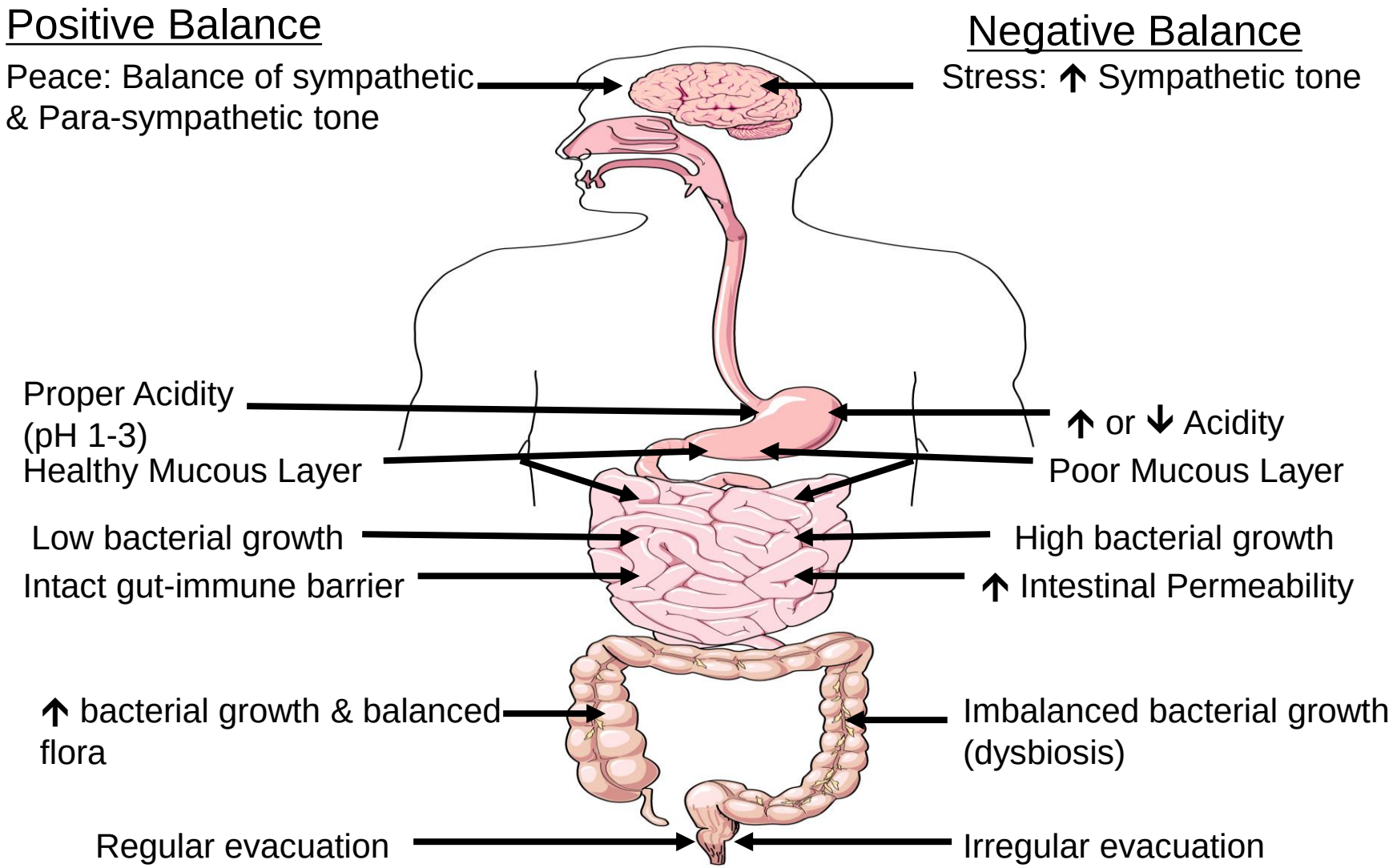
Carroccio, A., et al., *Non-celiac wheat sensitivity diagnosed by double-blind placebo-controlled challenge: exploring a new clinical entity.* Am J Gastroenterol, 2012. **107**(12): p. 1898-906

Celiac vs Non-Celiac Gluten Sensitivity

	CD	NCGS
Bowel pattern	More diarrhea	More constipation
Age	Presents later	Presents earlier
Serology (tTG IgA, DGP)	Positive	Negative
Symptoms of malabsorption (weight loss, diarrhea)	More common	Less common
Genetic Testing: HLA DQ2/DQ8 Note: this test is + in 40%. Negative test is most useful to rule out CD.	Order if serology borderline with symptoms of malabsorption. If negative=NCGS	Not needed if serology negative
Family History	Positive	Negative
Other Auto-immune Disease	Positive	Negative
Endoscopy and biopsy	To confirm CD	Rarely necessary

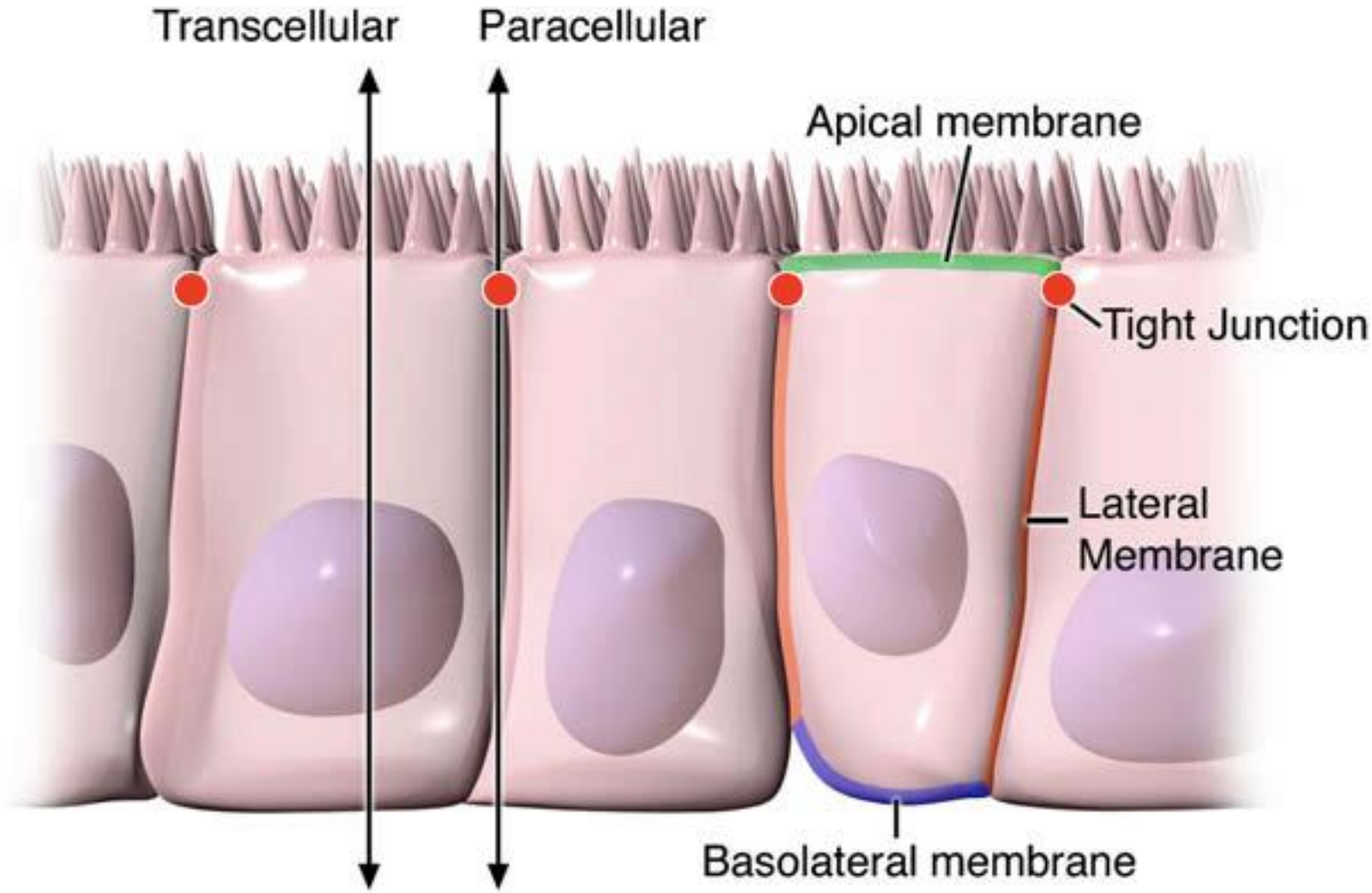
Kabbani, T.A., et al., *Celiac Disease or Non-Celiac Gluten Sensitivity? An Approach to Clinical Differential Diagnosis.* Am J Gastroenterol, 2014.

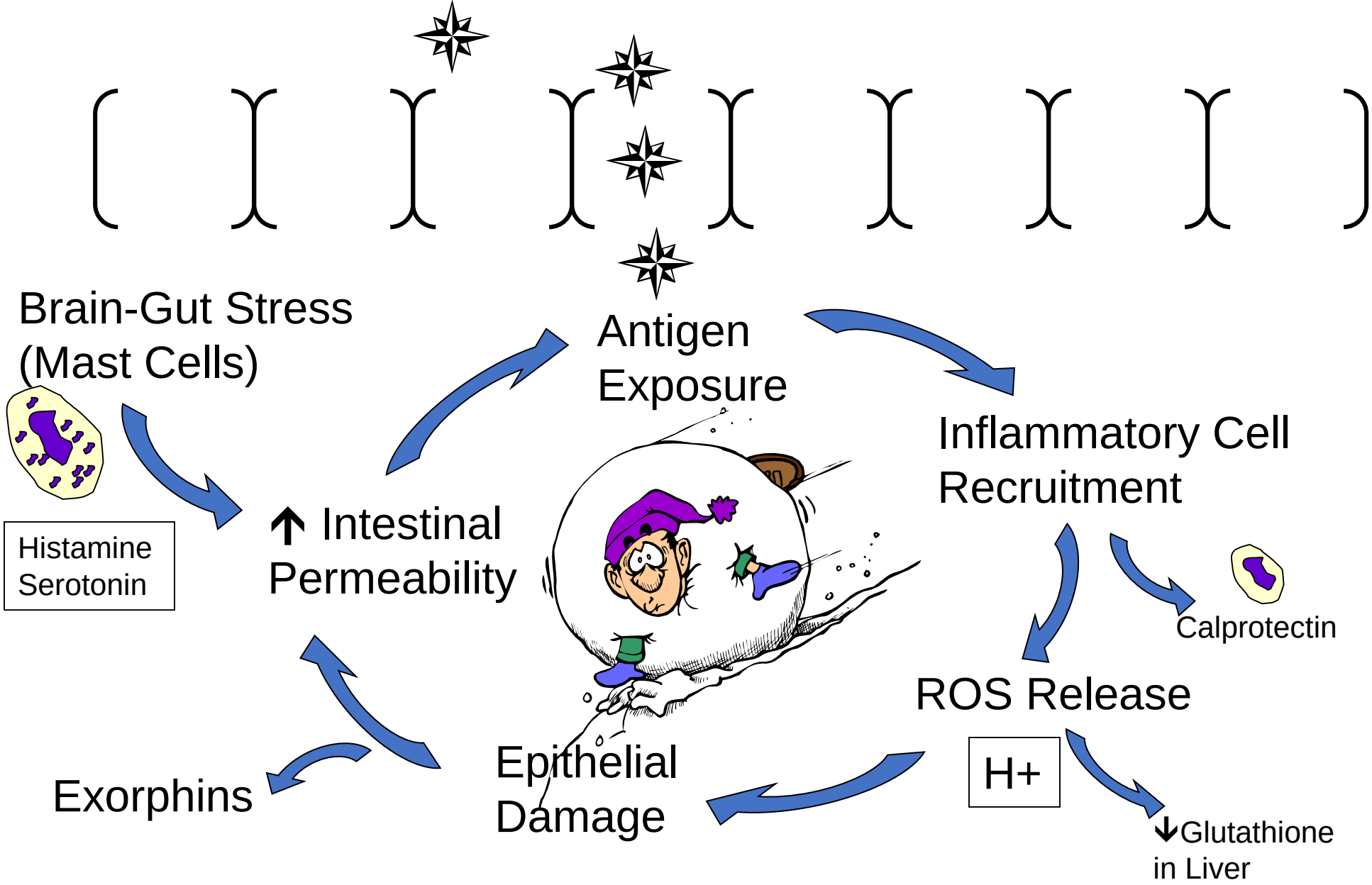
OPTIMAL HEALING ENVIRONMENT FOR THE G.I. TRACT



UW Health Integrative Medicine

The Enterocyte:
Regenerate every 3-5 days!

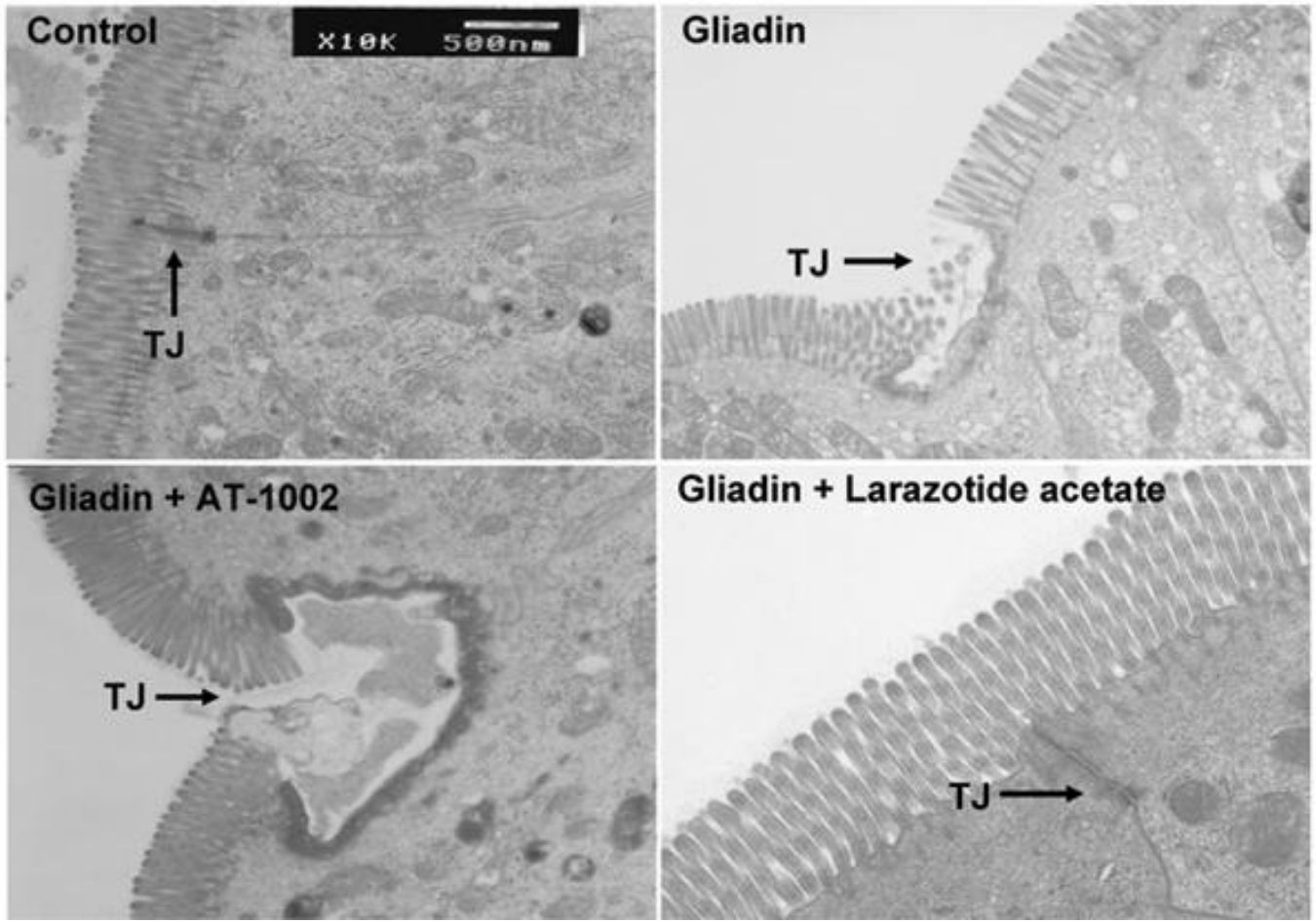




Farhadi A, Banan A, Fields J, Keshavarzian A. Intestinal barrier: An interface between health and disease. J Gastroenterol Hepatol. 2003; 18(5):479-497.

Rx to Watch: Larazotide

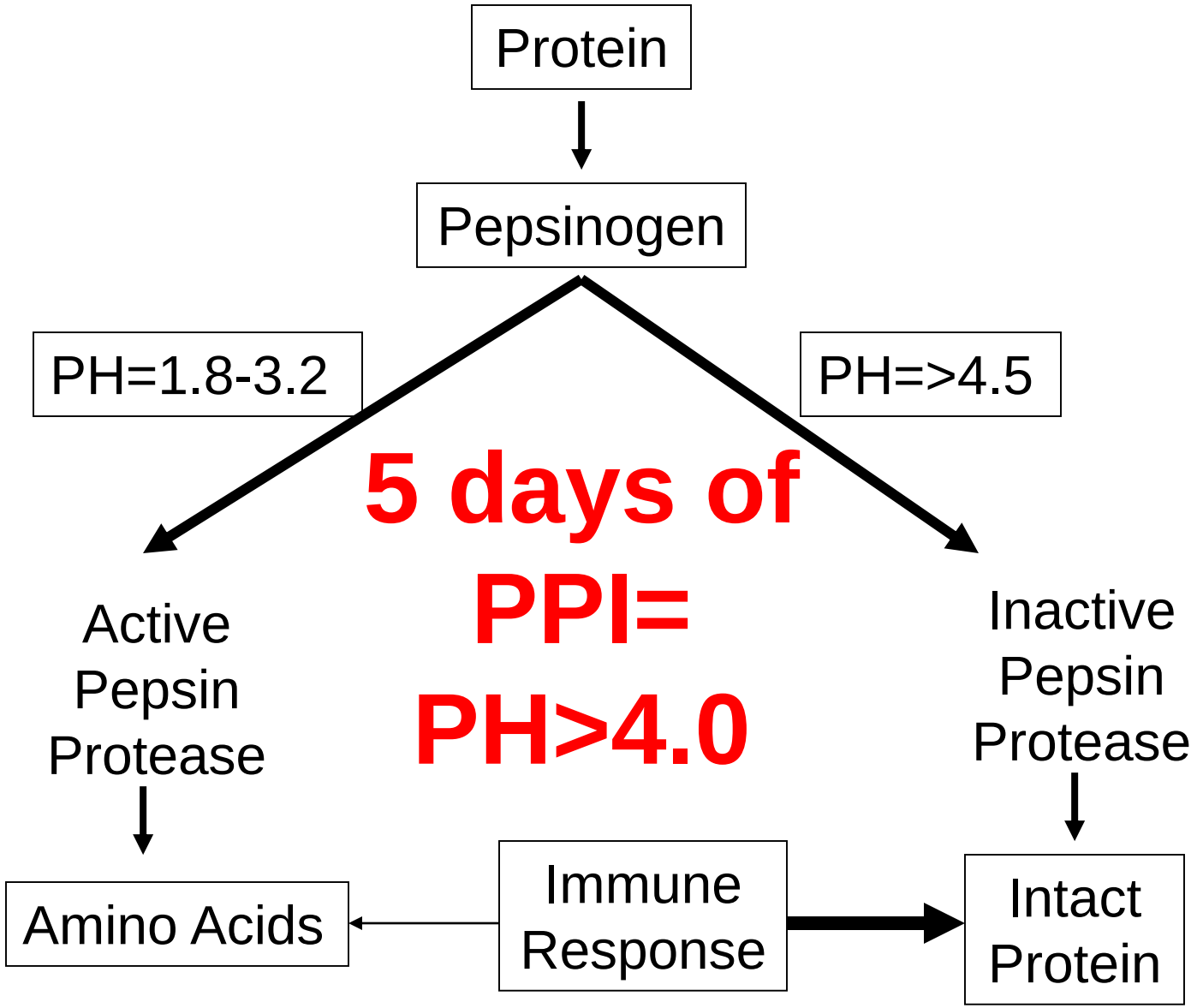
Leffler, D.A., et al., *Larazotide Acetate for Persistent Symptoms of Celiac Disease Despite a Gluten-Free Diet: A Randomized Controlled Trial.* Gastroenterology, 2015

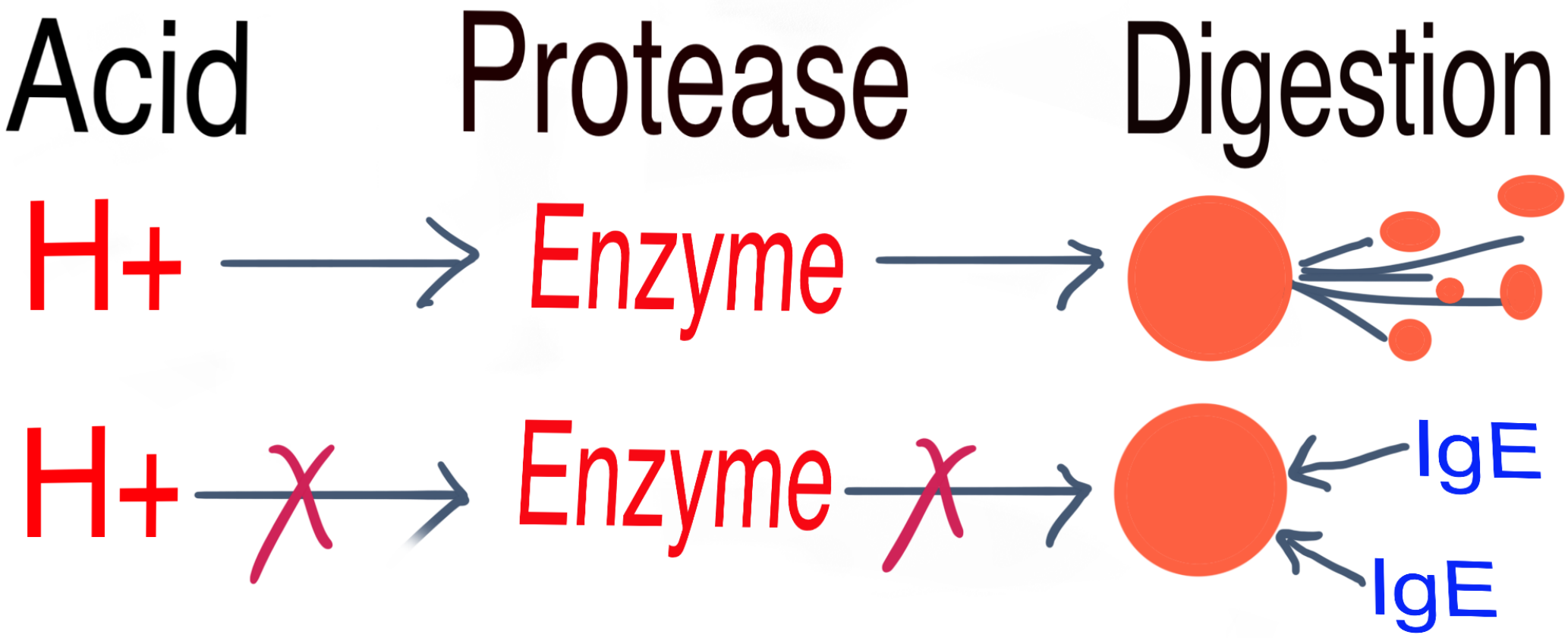


Gliadin + Rx Reduces intestinal permeability

Is there enough acid to stimulate digestion?

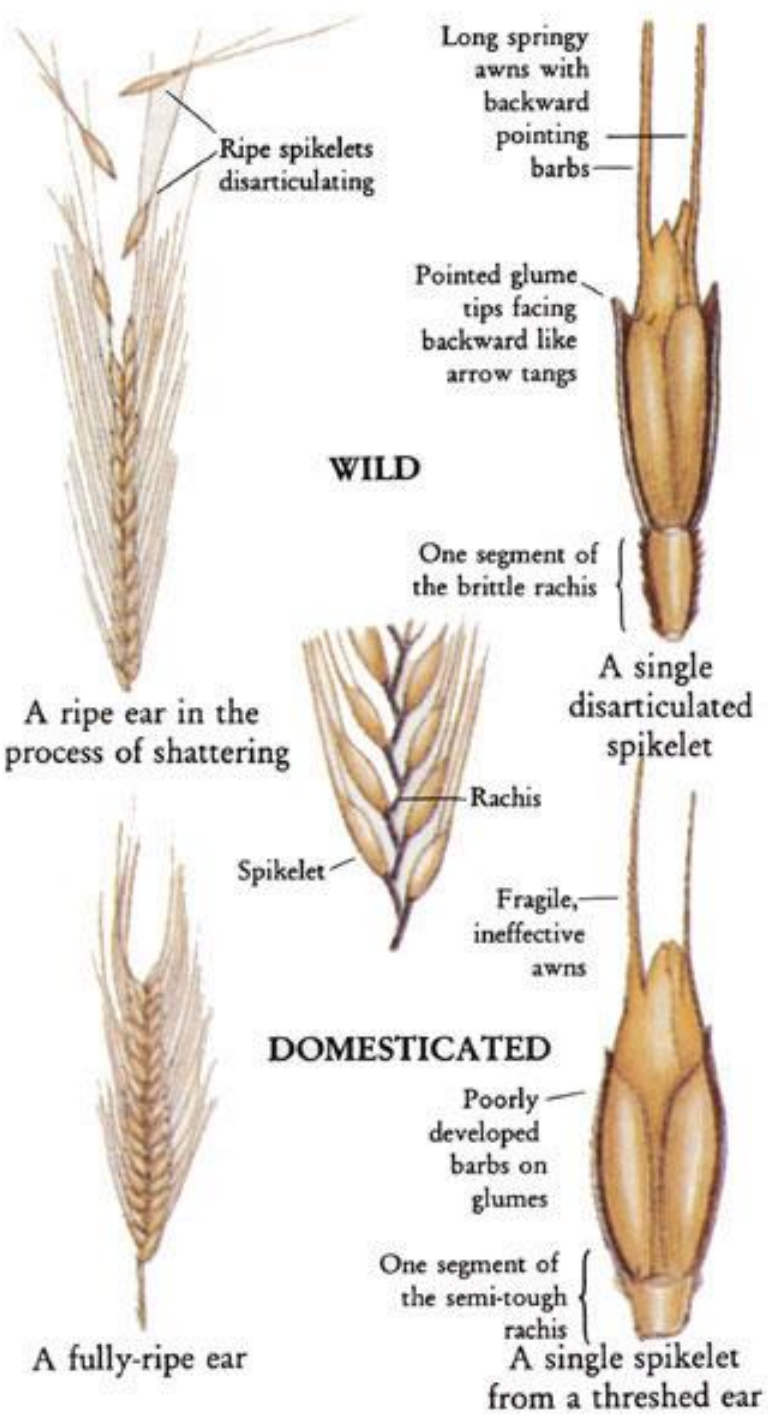
Acid Activates Pepsin




Acid
Protease
Digestion
H+
Enzyme
H+
Enzyme
IgE
IgE

Is there a food antigen that is activating inflammation?

Consider a two week elimination diet (see handout)



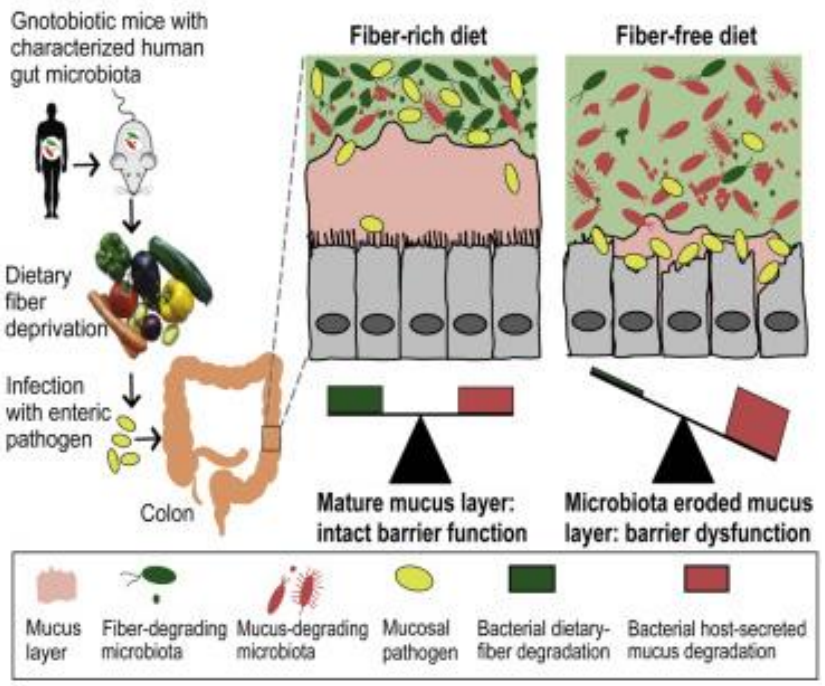
Domesticated Wheat:

- ✓ Hybridized
- ✓ > 40 chromosomes (vs 14)
- ✓ Short (dwarf)
- ✓ More gluten with more subtypes

Is there adequate mucous for the microbiome?

Fiber in moderation

- U of M study: 3 groups of mice
  - High fiber
    - Healthy gut lining
  - Fiber-free
    - Mucusal lining “drastically diminished”
  - Alternating qod
    - Mucus layer half as thick of high-fiber group



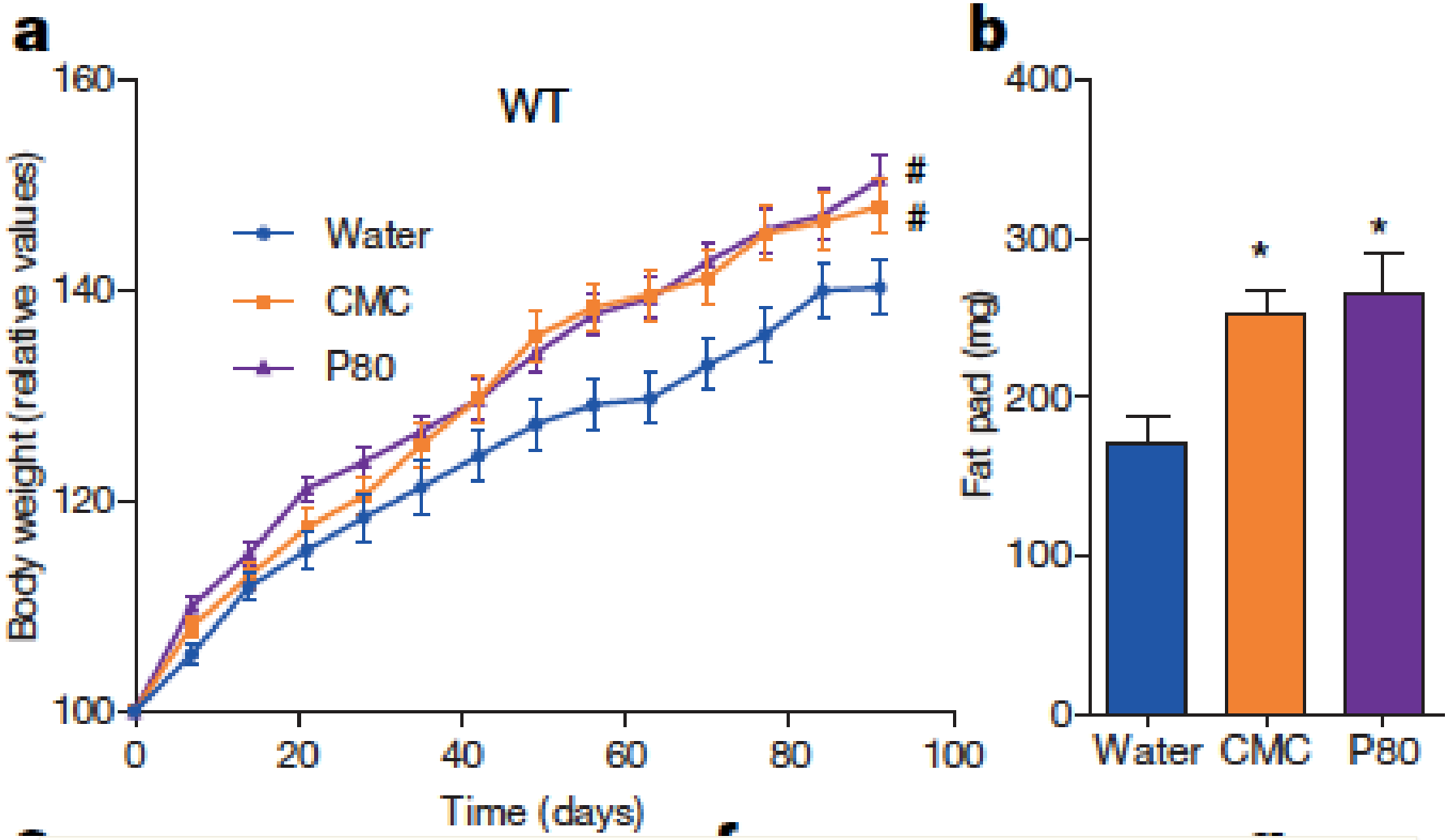
Desai MS, Seekatz AM, Koropatkin NM, et al.. A dietary fiber-deprived gut microbiota degrades the colonic mucus barrier and enhances pathogen susceptibility. *Cell.* 2016;167(5):1339-1353.

Water with Soluble Fiber! (psyllium, guar gum, ground flax, etc.)

Parretti et al. Efficacy of water preloading before main meals as a strategy for weight loss in primary care patients with obesity: RCT. Obesity 2015;23:1785-91.

1. Reduces absorption of cholesterol
2. Slows absorption of sugar lowering glycemic index.
3. Absorbs water and slows digestion stimulating satiety (wt. loss)

Mucous protects intestines



Chassaing, B., et al., *Dietary emulsifiers impact the mouse gut microbiota promoting colitis and metabolic syndrome.* Nature, 2015.

Useful tests?

- Stool analysis with parasites
- Pancreatic elastase (enzyme status)
- Fecal calprotectin (inflammation)
- Gastric ph (acid status)
- Hydrogen breath test (SBBO)
- EGD (Barrett's?)
- On PPI? Check B12, Fe, calcium, mg, gastrin.

Therapeutic IBS Summary

- Ever since that illness, Abx or sentinel event=IBS:
  - 4 R approach (See handout)
- Chronic IBS:
  - #1Mind-body tools (hypnosis, CBT)
  - Exercise
  - Trial of elimination diet/improve nutrition
  - Fiber (Guar Gum, Psyllium, ground flax)
  - Peppermint Oil: 0.2-0.4 ml enteric coated capsules TID
  - Cromolyn (Gatrocrom) 400 mg TID
    - Best if + response to elimination diet

Fred, 64 yo retired UNM Executive

Patient with HTN, dyslipidemia and type II DM presents with loss of his “get up and go.” He has had a stent placed for a narrowing of his LAD from a cath that he had because of an abnormal exercise stress test. He is on Metformin, Esomeprazole, Lisinopril and high dose statin. He has a hx of low vitamin D levels at 18 ng/dL which he supplements with 3000 IU of D3 daily.

Handout Tools

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- FODMaPs
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- How to taper off a PPI
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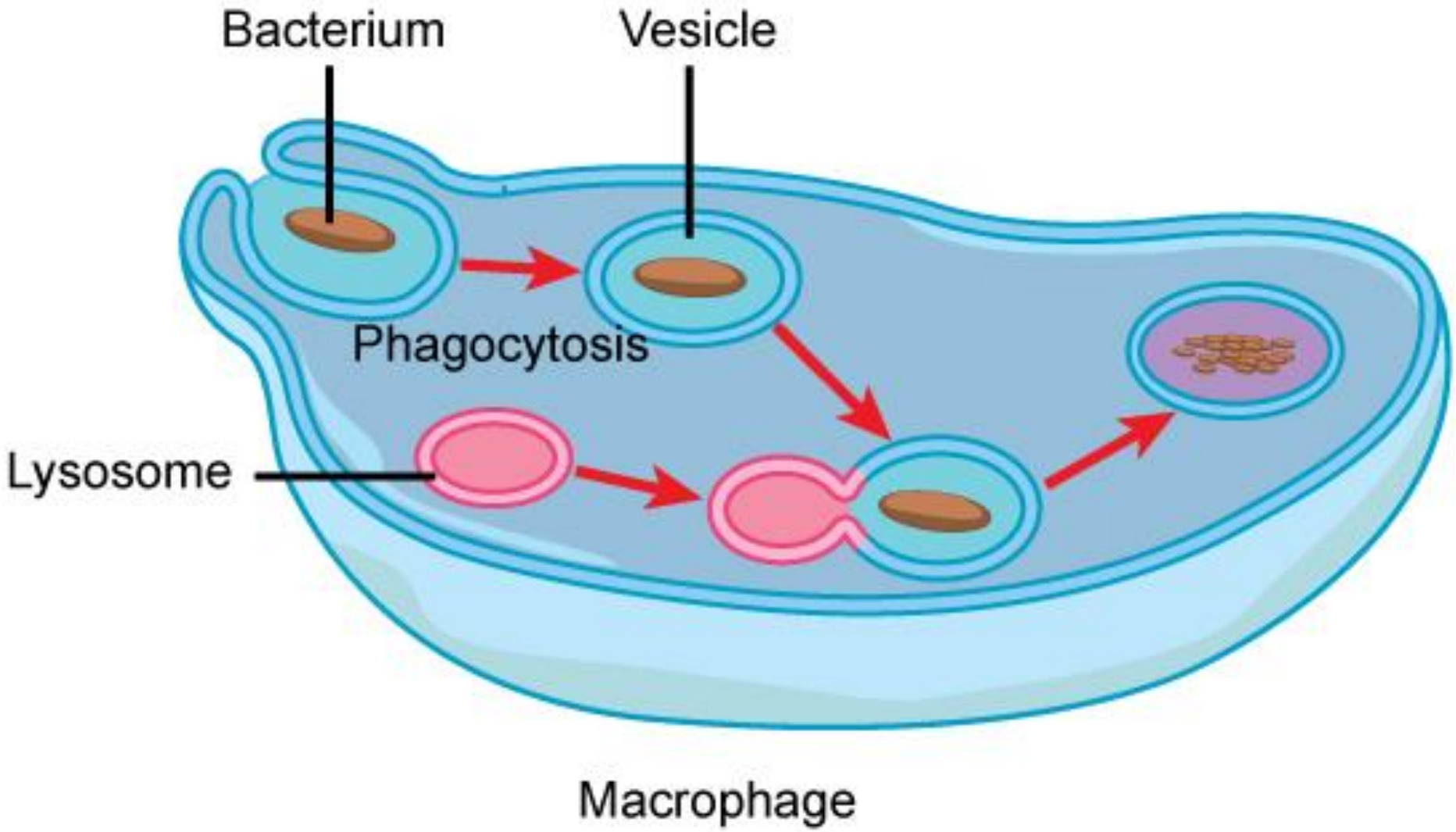
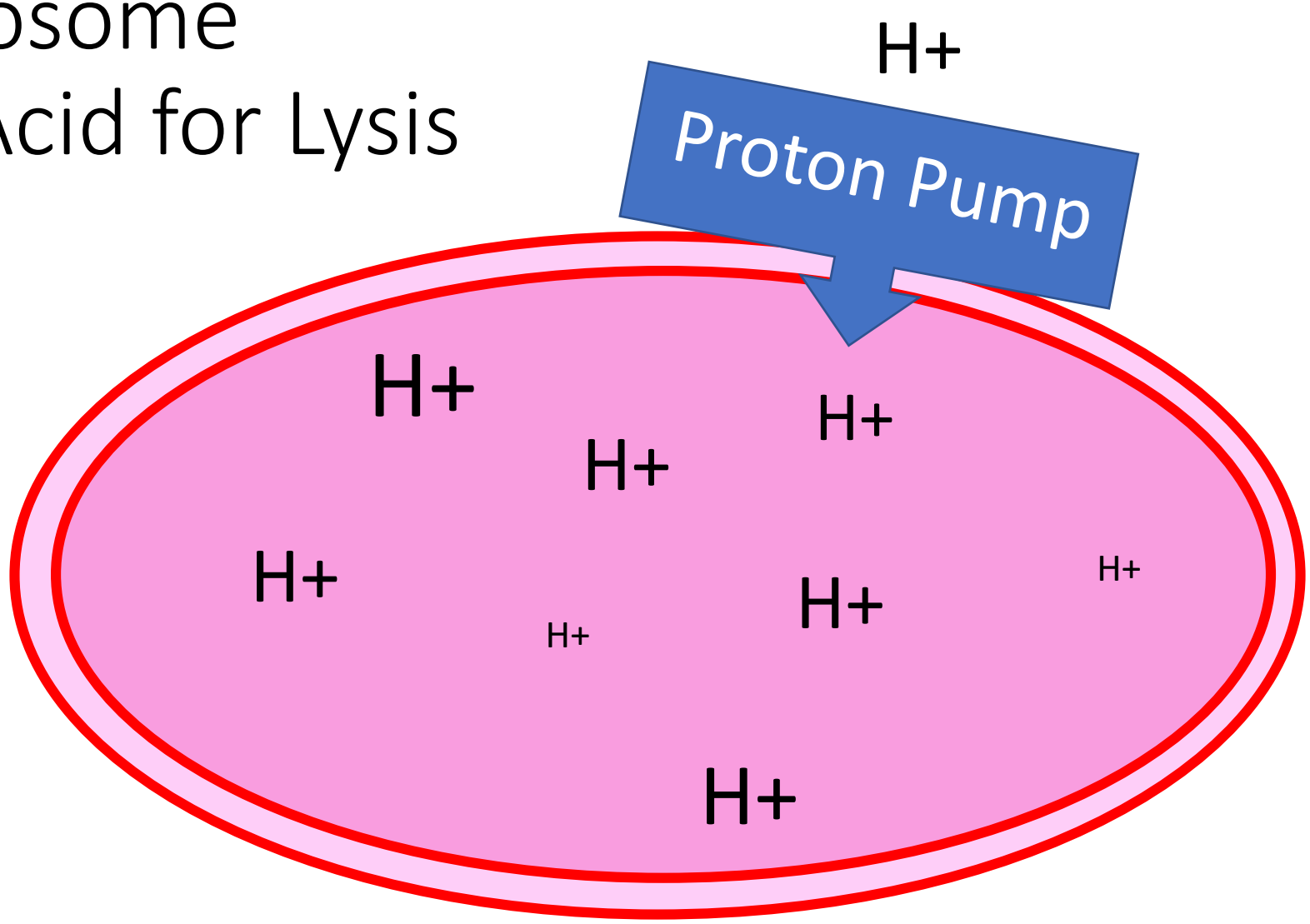
- Breathing Exercises (Vagal Nerve Stimulation)

Iron malabsorption/anemia[11]	**HCL releases non-heme iron from its fiber carrier and then dissolves it.**
Magnesium malabsorption/cardiac arrhythmia[12]	Long term use of PPI is associated with greater risk. Mg levels can return to normal after one week of stopping PPI. Can cause cardiac arrhythmia, tremor and seizures if low.
Cardiac Mortality[13]	Data mining study of 1.8 million patients showed 1.2 risk of MI and 2.0 risk of cardiac mortality. Possibly related to inhibition of DDAH & ADMA enzymes needed to activate nitric oxide in the endothelium.
Chronic Kidney Disease[14]	Daily PPI use associated with a 1.24 risk of chronic kidney disease. Twice daily PPI uses associated with a 1.46 risk. May share similar MOA as CV risk above.
Dementia[15]	Possible increased risk of beta-amyloid production. Increased incidence of dementia in 73,679 participants 75 years of age or older using PPIs
Stroke[16]	Increased risk with length of time on and dose of PPI but not seen with H2 blockers.
Hepatic Encapholopathy[17]	Increased risk in patients with cirrhosis related to PPI induced gastric dysbiosis.


Bacterium
Vesicle
Phagocytosis
Lysosome
Macrophage

The Lysosome Needs Acid for Lysis



Chronic PPI Use

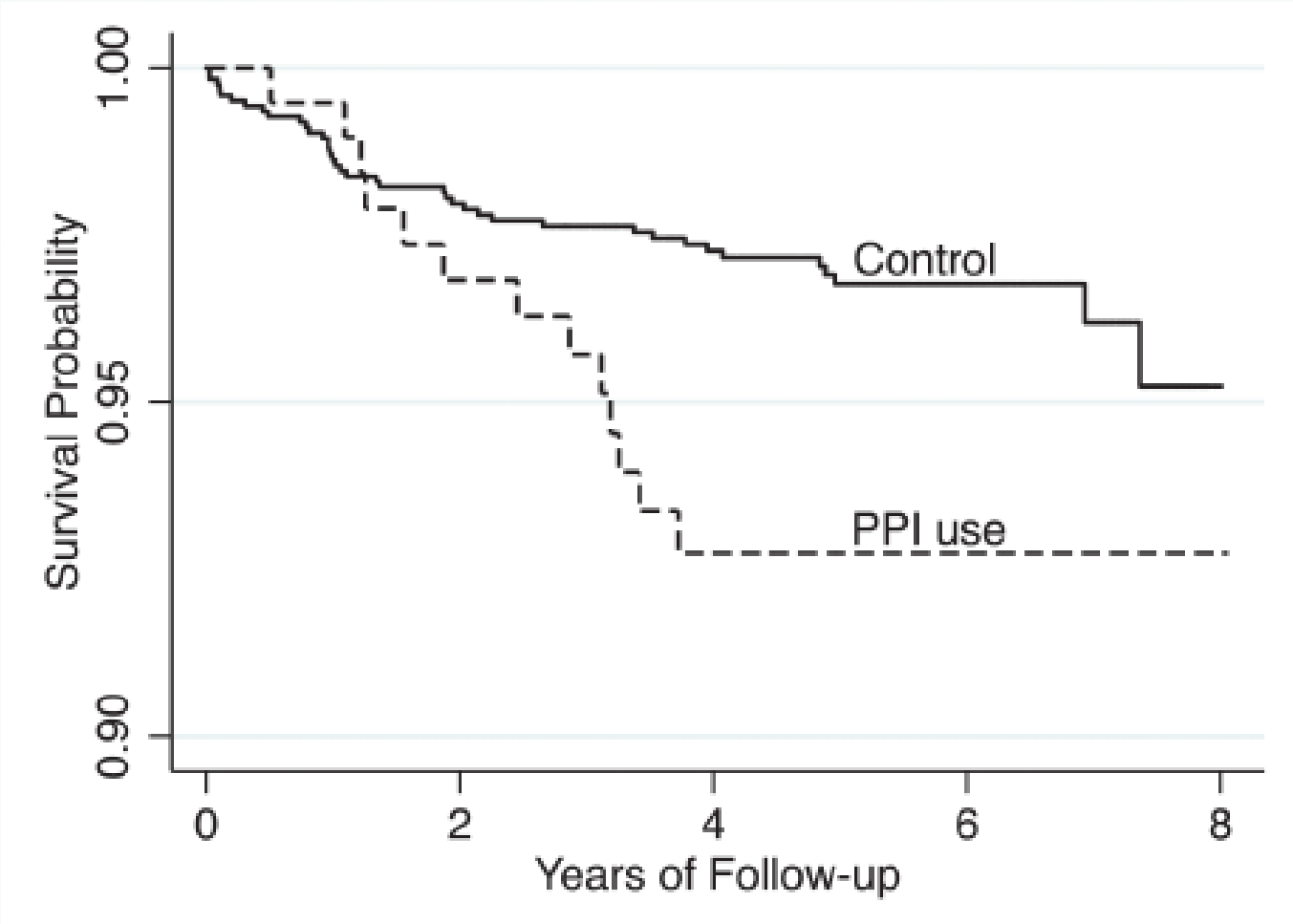
1.8 million patients, a trillion bits of data!

1.2 x risk of MI

2.0 x risk of cardiac mortality

MOA: Blocks enzymes (DDAH, ADMA) needed to produce nitric oxide

Shah, N.H., et al., *Proton Pump Inhibitor Usage and the Risk of Myocardial Infarction in the General Population.* PLoS One, 2015. **10**(6).



Shah, N.H., et al., *Proton Pump Inhibitor Usage and the Risk of Myocardial Infarction in the General Population.* PLoS One, 2015. **10**(6)

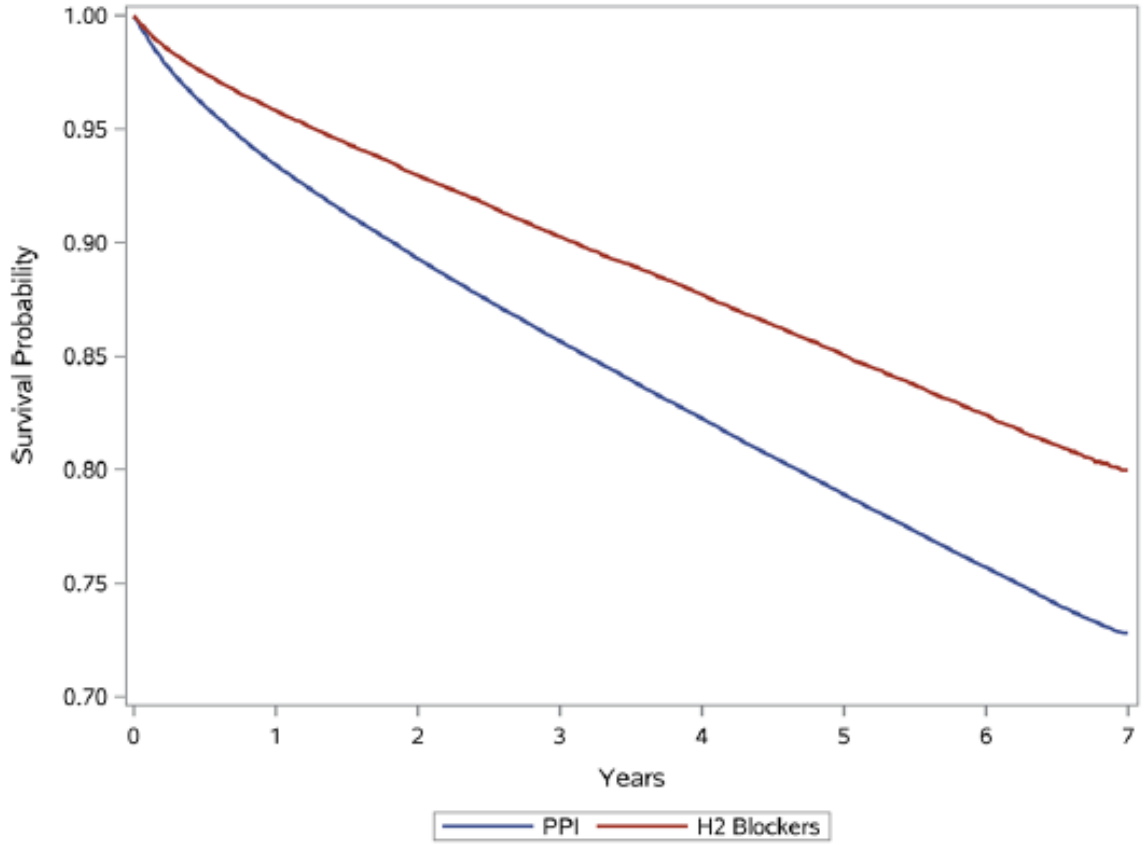


Figure 1 Survival curves for PPI and H2 blockers. PPI, proton pump inhibitor.

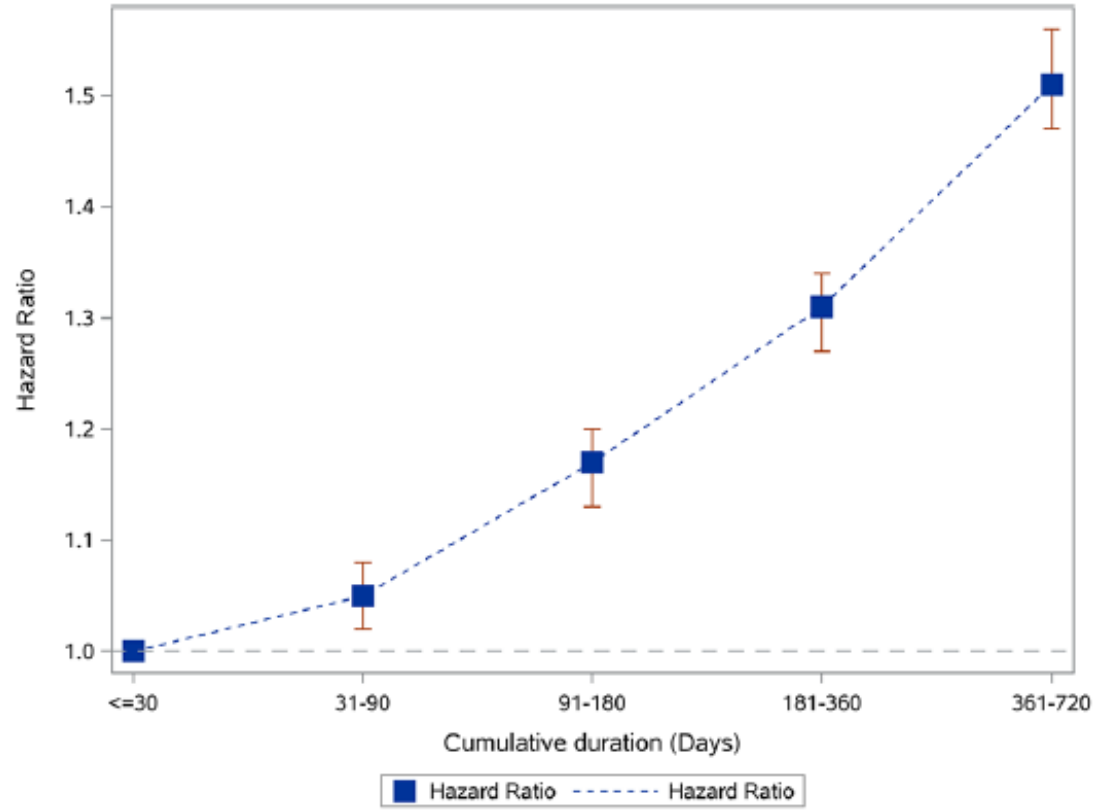
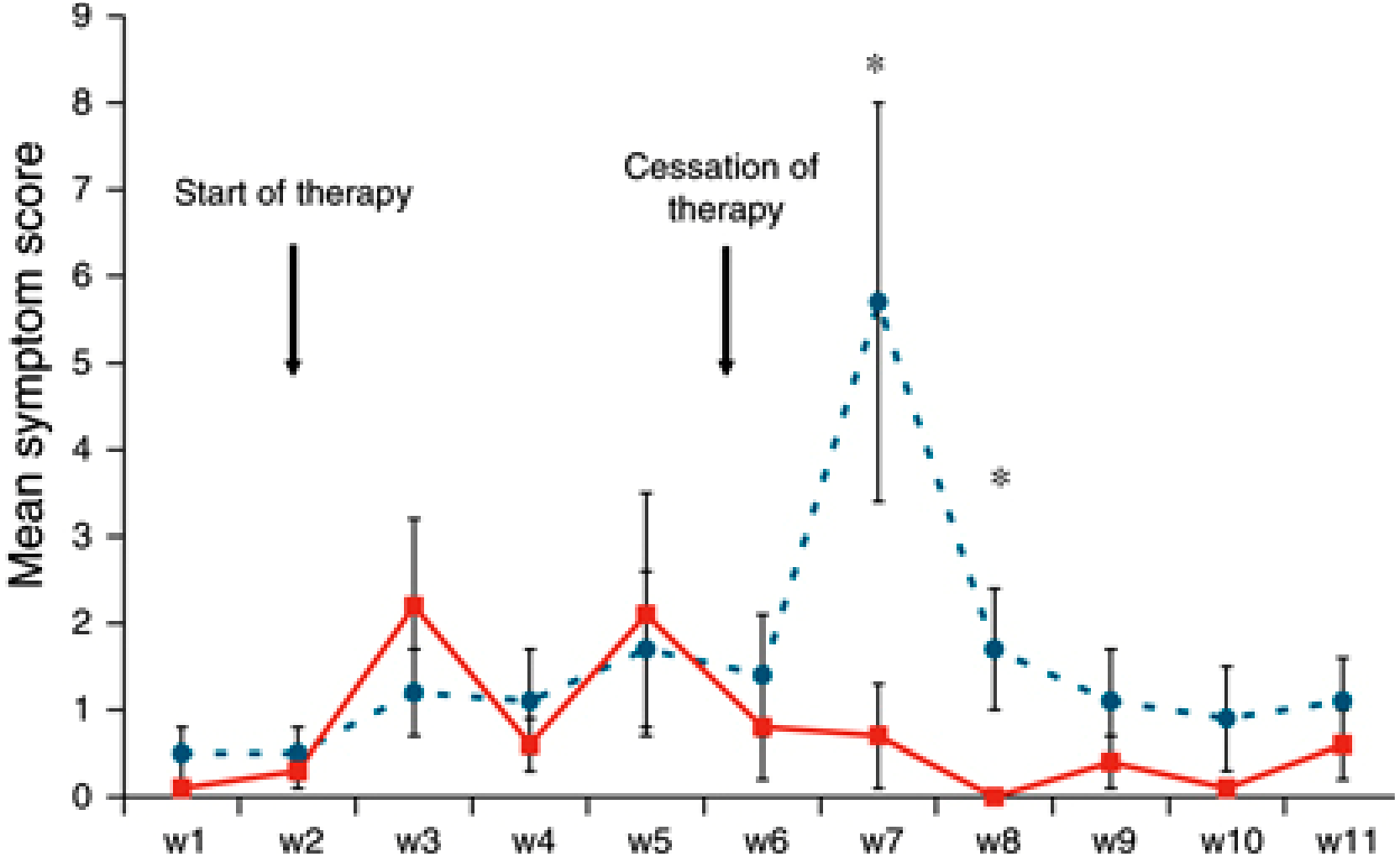


Figure 2 Duration of PPI exposure and risk of death among new PPI users (n=166 098). PPI, proton pump inhibitor.

Xie, Y et all. Risk of Death among users of Proton Pump Inhibitors: a longitudinal observational cohort study of United States Veterans. BMJ Open. 2017.

Rebound Dyspepsia W/ D/C of PPI



Niklasson A, et al. Dyspeptic symptom development after discontinuation of a proton pump inhibitor: A double-blind placebo-controlled trial. Am J Gastroenterol. 2010.

How to Taper Off a PPI

- Improve nutrition (caffeine, carbonated beverages, sugary drinks, fat)
- Address emotional stressors/Breathing Exercises
- Taper to lowest dose of PPI before D/C
- Bridge for two weeks with
  - Acupuncture
  - Sucralfate 1 gm with meals and at bedtime
  - DGL (De-Glycerheizinated Licorice)
  - Melatonin before bed if symptoms are at night (strengthens LES)
- If symptoms persist beyond 3 weeks, repeat EGD and consider H2 blocker which is safer than a PPI

Rx and Nutrient Deficiencies

First do no Harm

Aroda, V.R., et al., Long-term Metformin Use and Vitamin B12 Deficiency in the Diabetes Prevention Program Outcomes Study. J Clin Endocrinol Metab, 2016

Drug	Depleted Nutrient	Notes
Metformin	B12, Folate, Thiamine (B1)	Elevated homocysteine suggests more severe B-Vit deficiency in the tissues
Proton Pump Inhibitors	B-vitamins, Mg, Iron, Calcium, Zinc, Vit C, Chromium	We need acid to absorb many key nutrients
ACE Inhibitors	Zinc	Think, “ACE to Zinc.” Be concerned in elderly with recurring infections or those with acne as zinc is needed to fight infections
Thyroid hormone	Calcium	Helps explain osteoporosis risk with over-treatment
Acetaminophen	Glutathione	The main amino acid that fuels health and repair of the gut lining (enterocytes)
Statins	Co-enzyme Q 10	The “spark plug” of the mitochondria which may explain the risk of myositis
Insulin	Magnesium	Check levels in diabetics with cardiac arrhythmias. Red blood cell levels are more accurate than serum levels.

The power of positive expectation, support and compassion……