

Microbiome: What it Is and Why It's Important to Your Health

Celebrating a Second Chance at Life
Survivorship Symposium

April 27 – May 3, 2024



Urv A. Shah MD

Assistant Attending Physician,
Myeloma Service, Memorial Sloan
Kettering Cancer Center



Microbiome: What It is and Why It's Important to Your Health

Urvi A. Shah, MD

Assistant Attending, Myeloma Service

@UrviShahMD

April 29, 2024



Memorial Sloan Kettering
Cancer Center

Disclosures

Research Funding (to institution)

BMS

Janssen

Sabinsa

M and M labs

Advisory Board

Janssen

BMS

Sanofi

Honoraria

MJH Life Sciences

Janssen

MashUpMD

RedMedEd

i3Health

Medscape

Medical Advisory Board (uncompensated)

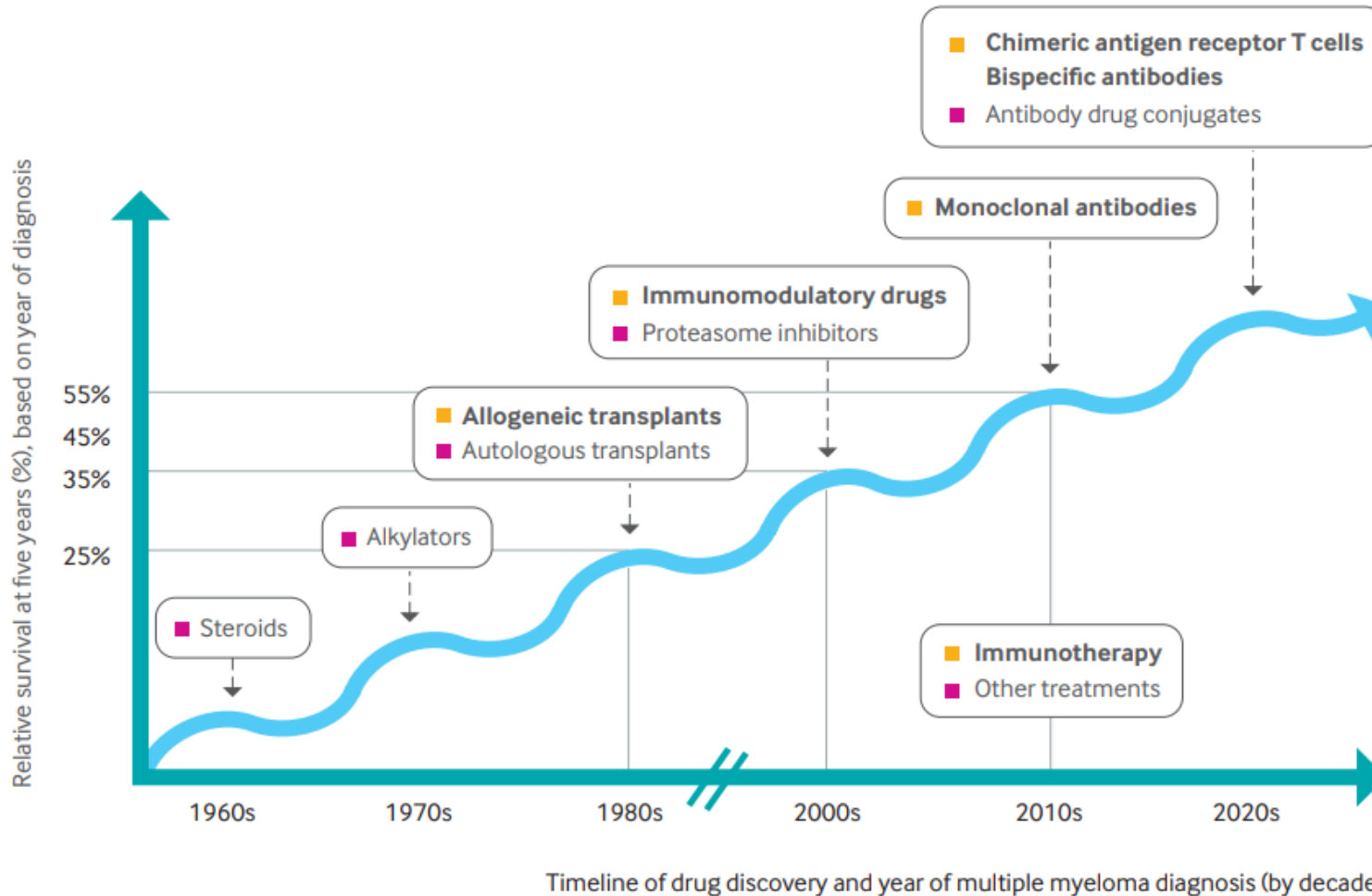
Plant Powered Metro New York

Nutrition Intervention (NUTRIVENTION) Research at MSK

Research program at MSK to study nutrition, microbiome and metabolism in myeloma.



Patients with blood cancers are living longer than before



There is an opportunity to improve outcomes and quality of life further with dietary and lifestyle interventions.

Shah UA, Mailankodv S. *BMJ* 2020

66-year-old male with multiple myeloma

Past Medical History

Coronary Artery Disease

Atrial fibrillation

Neuropathy

Hypertension

Hyperlipidemia

Stroke with weakness in wheelchair

Deep vein thrombosis

Sleep apnea

Morbid Obesity

Major depressive disorder

Frequent hospital admissions

Cognitive decline/dementia

Degenerative joint disease

Cellulitis

Abdominal hernia

- Kidney stone
- Hyperthyroidism
- Multifocal pneumonia
- Type 2 DM
- Congestive heart failure
- Prolapsed eye
- left lower lymphedema from CABG.

Past Surgical History

- Right knee repair
- Right knee joint replacement surgery
- Umbilical hernia repair
- Tonsillectomy x 2
- Cardioversions x 10
- Multiple cardiac ablation.
- Coronary Artery Bypass Graft

Therefore, not a candidate for:
Stem cell transplantation
CAR T cell therapy
Clinical trials
Some intensive chemotherapy

Thus, decreased overall survival.

75-year-old male with multiple myeloma

IgG kappa and free kappa
ISS stage I, RISS stage I
multiple myeloma

Treated with 6 cycles of
daratumumab, lenalidomide
and dexamethasone

Followed by lenalidomide
maintenance

Achieved complete response

Past Medical History

Coronary Artery Disease

Atherosclerosis

Hyperlipidemia

Prediabetes

Depression

Past Surgical History

Gall bladder removal surgery

**Although multiple myeloma was
in remission, patient died of a
cardiac arrest.**

Outline

Lifestyle Considerations

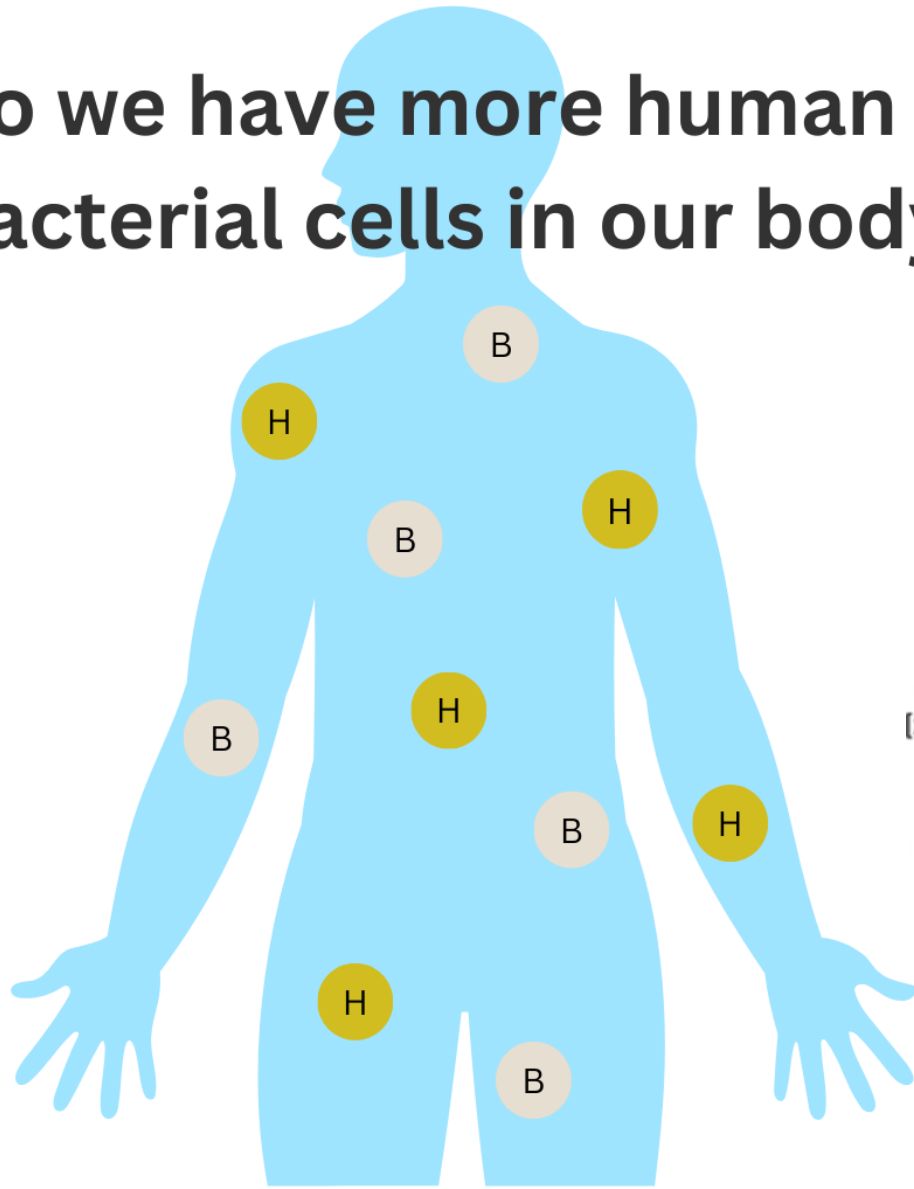
Research

- Microbiome
- Dietary Patterns
- Interventional Trials –
 - Prevention
 - Treatment
 - Survivorship
 - Comorbidities

Practical Nutrition Tips

Some Myths

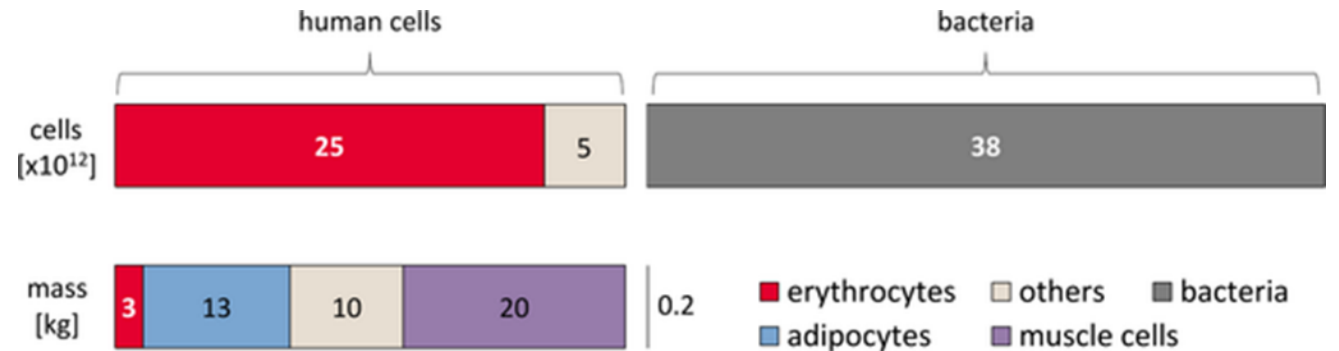
Do we have more human or bacterial cells in our body?



Number of human and bacterial cells in the body

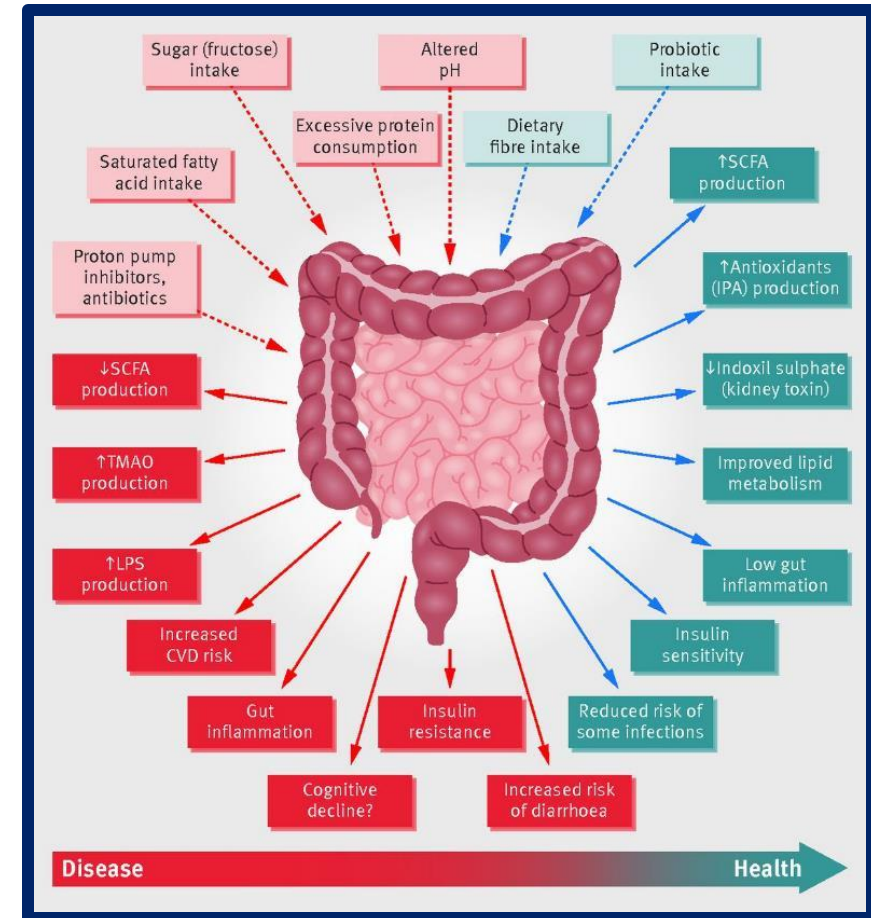
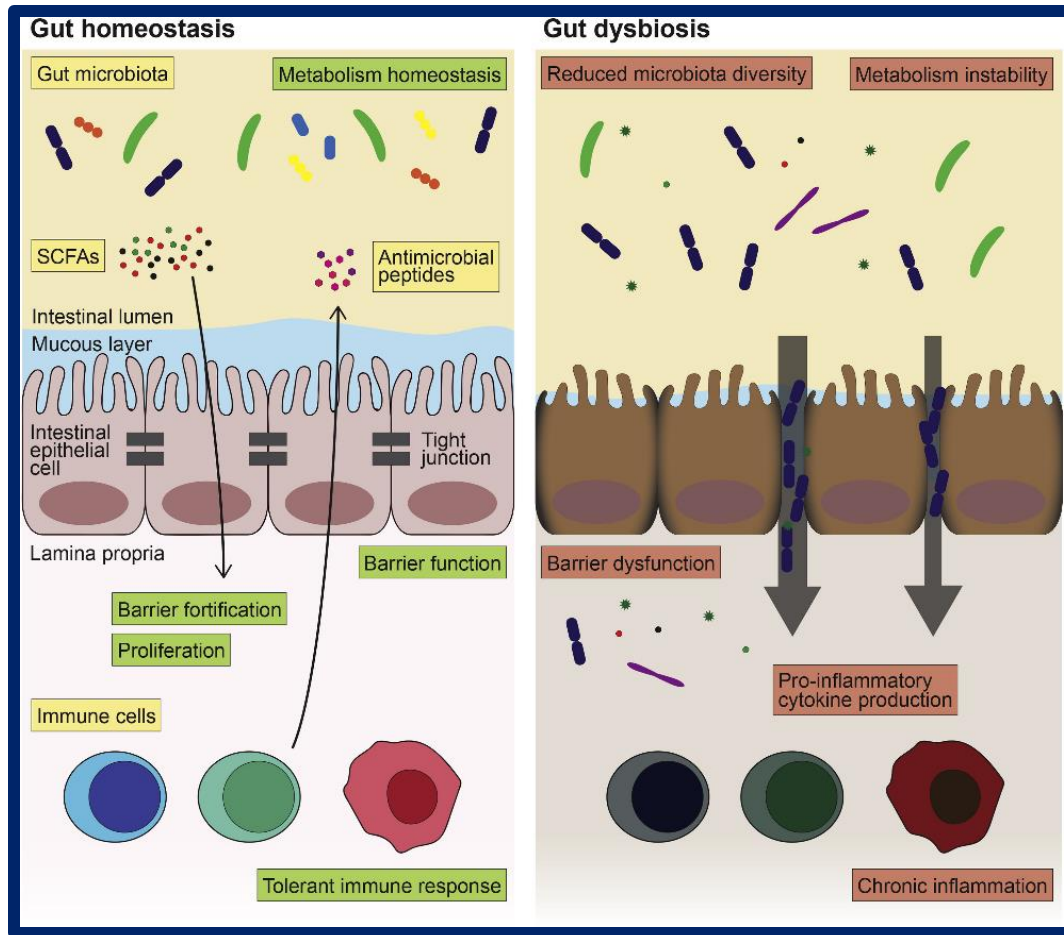
Human = 30 trillion

Bacteria = 38 trillion



Sender et al. PLOS Biology 2016

Microbiome in Health and Disease



Kim et al. *Trans Med Aging* 2020; Valdes et al *BMJ* 2018

Factors That Influence Microbiome

Non-Modifiable Factors

Age
Gender
Race/Ethnicity
Genetics
Infections
Vaccination
Medical Conditions
Cancer
Rural/Urban Environment

Modifiable Factors

Nutrition/Dietary Patterns
Obesity
Diabetes Mellitus
Physical Activity
Sleep
Stress
Smoking/Alcohol/Drugs
Medications

What is Microbiome Diversity?

- **Gut microbiome alpha diversity:**
Diversity of bacterial species within the gut microbiome of the same individual



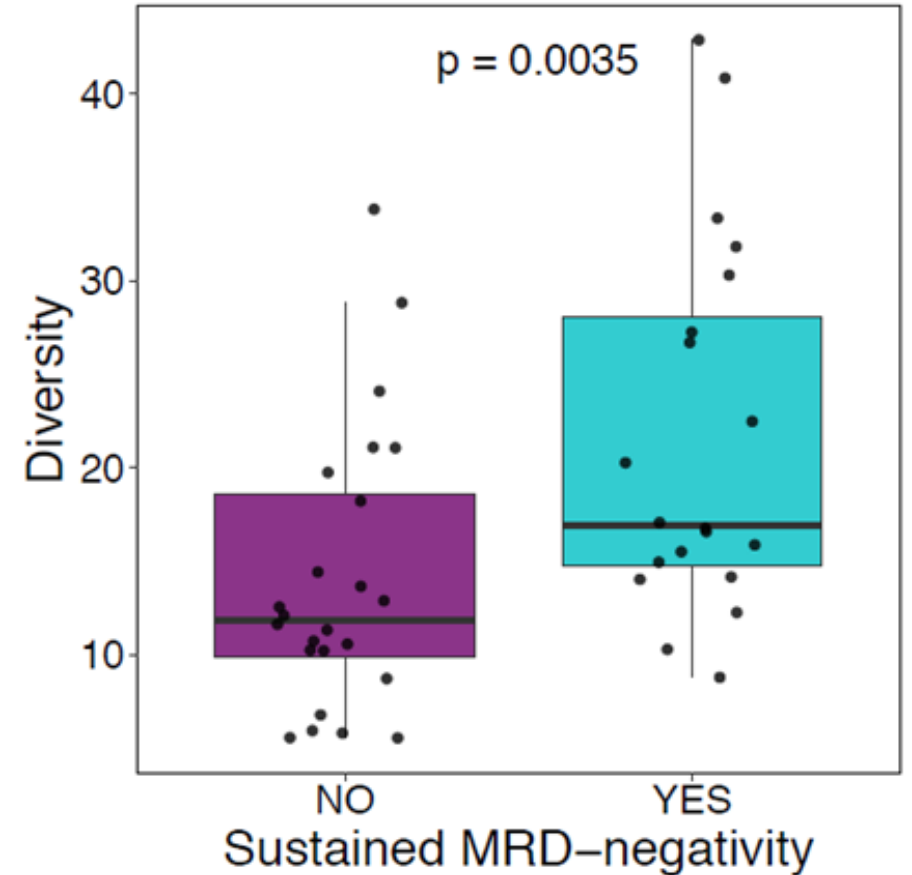
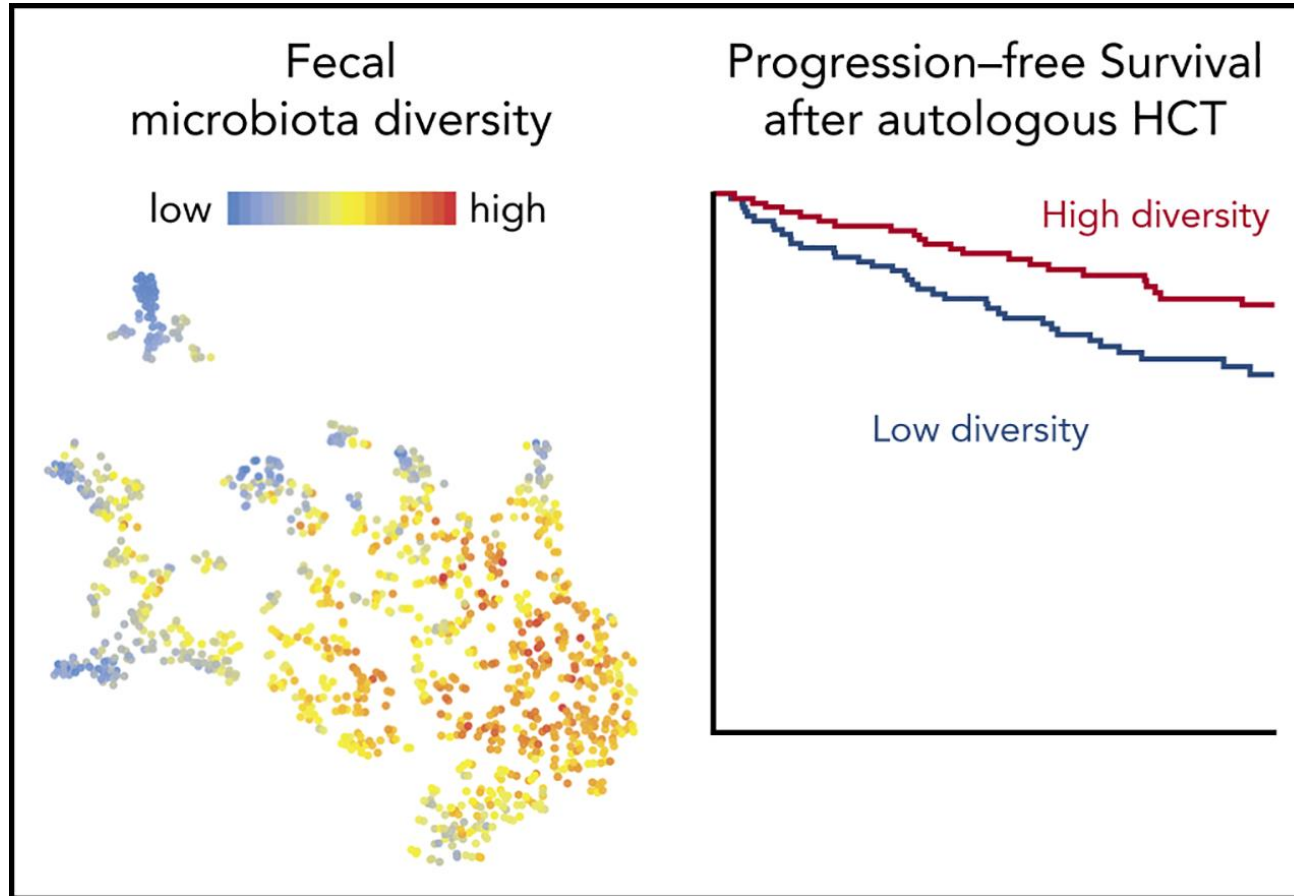
A **healthy forest** has many varieties of flora and fauna, big and small.

vs.



A **plantation**, on the other hand has just a couple of different trees generally in the same size.

Microbiome Diversity is associated with Survival



Khan et al. Blood 2021; Shah UA et al. Clin Can Res 2022

Want to improve your gut
microbiome diversity?



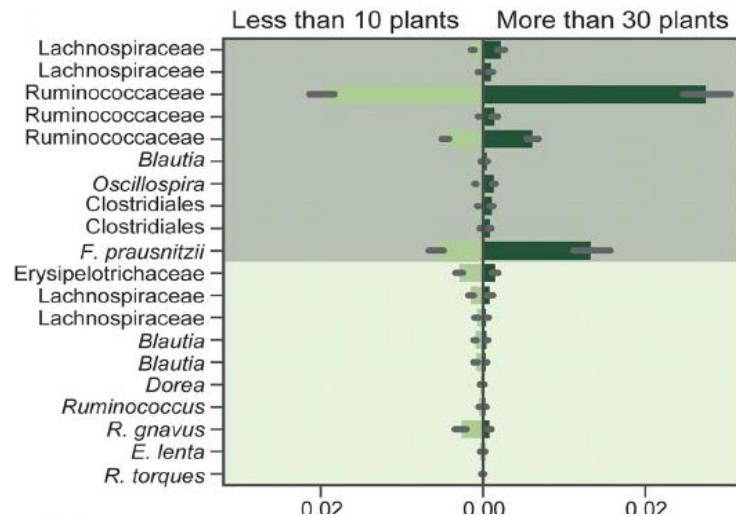
**Dietary patterns are a
modifiable factor that can
affect gut microbiome health**

How Many Different Plant Foods Do You Eat in a Week?

Stool samples from >10,000 individuals

>30 plant foods associated with

- ↑ Microbiome diversity
- ↓ Antibiotic resistance genes
- ↑ Conjugated linoleic acid abundance (polyunsaturated fatty acid with anti cancer and fat reducing properties)



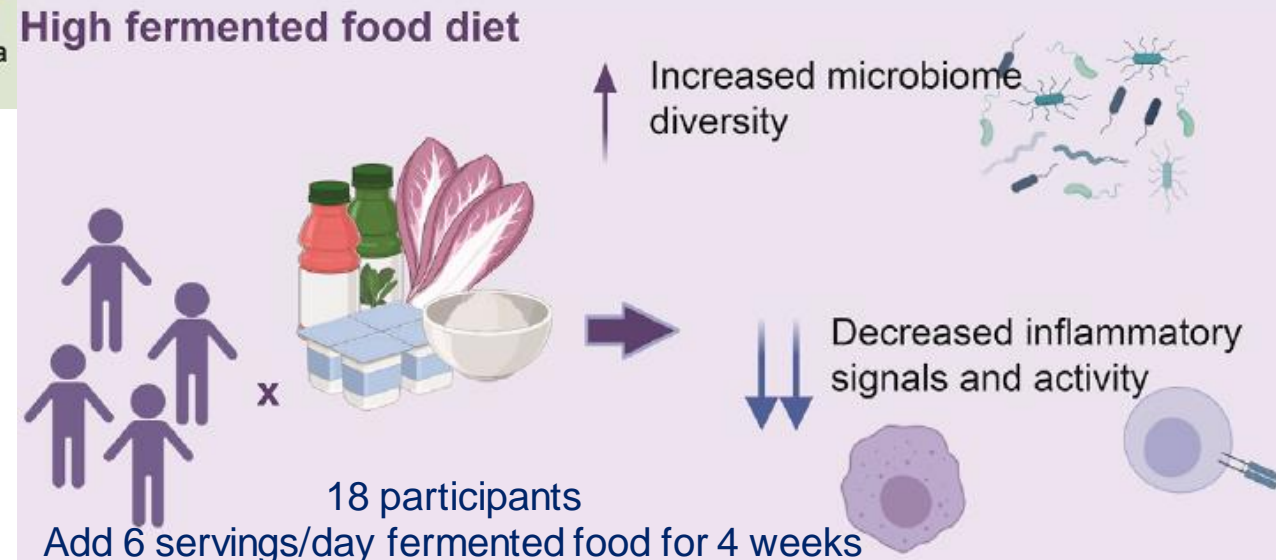
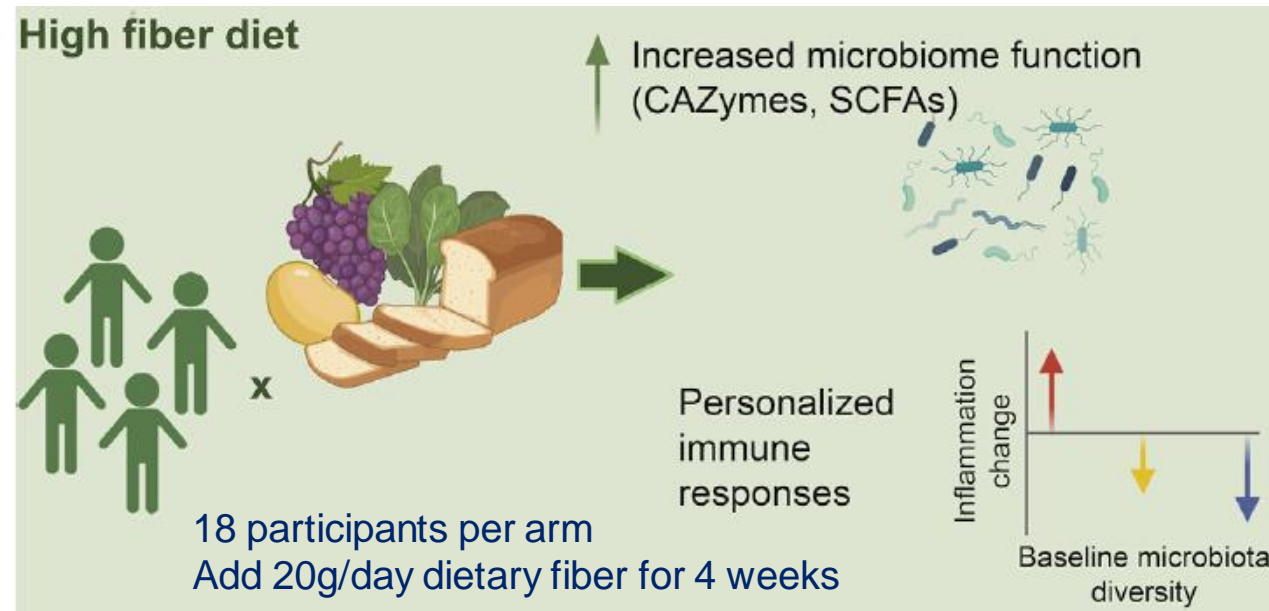
AIM TO EAT 30+ VARIETIES OF PLANT FOODS



McDonald et al mSystems 2018

Dietary Patterns Affect the Immune System

Studies in healthy populations show that dietary changes affect the immune system



Wastyk et al. Cell 2021

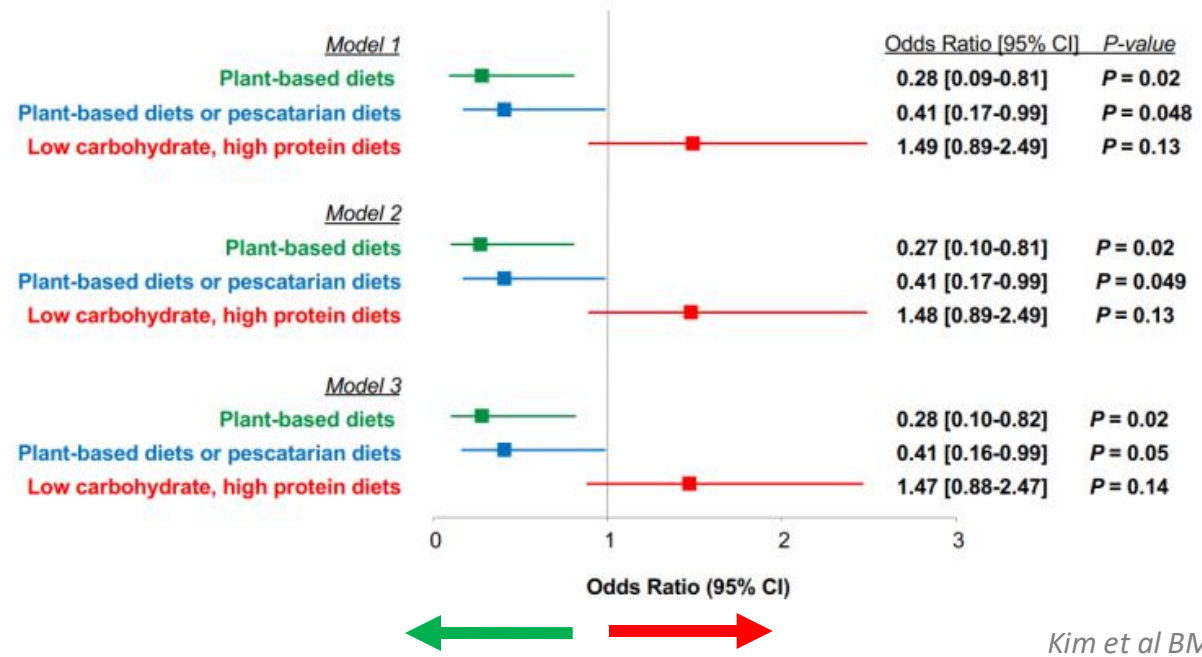
Diet and COVID19 Severity

Table 2 Dietary intake of healthcare workers stratified by self-report of following plant-based diet among COVID-19 cases (n=568)*

	Followed plant-based diet (n=41)	Did not follow plant-based diet (n=527)	P value
Dietary intake, times/week (mean, SD)			
Total fruits	9.8 (6.4)	8.5 (6.5)	0.23
Total vegetables	14.5 (8.7)	10.4 (7.1)	<0.001
Potatoes	2.1 (1.9)	2.1 (1.8)	0.90
Legumes	3.7 (2.9)	1.9 (1.6)	<0.001
Nuts	3.5 (2.6)	2.3 (2.9)	0.01
Refined grains	7.5 (5.5)	8.6 (5.2)	0.17
Dark or whole grain breads	2.5 (2.2)	2.2 (2.5)	0.55
Sweets and desserts	5.8 (5.8)	6.8 (6.9)	0.35
Eggs	2.0 (1.8)	2.3 (1.9)	0.30
Dairy	12.9 (9.1)	13.3 (7.9)	0.73
Poultry	1.2 (1.5)	2.3 (1.6)	<0.001
Red and processed meats	1.3 (2.3)	3.8 (2.8)	<0.001
Fish and seafood	2.5 (2.7)	3.1 (2.6)	0.12
Soups	1.4 (1.7)	1.4 (1.4)	0.78
Croquettes, dumplings, pizza	0.8 (0.8)	1.0 (1.0)	0.14
Sugar-sweetened beverages	1.1 (2.1)	2.5 (3.4)	0.01
Fruit juices	0.4 (0.9)	1.0 (1.9)	0.06
Vegetable oil	3.6 (3.3)	3.8 (3.2)	0.67
Butter	1.4 (2.0)	1.9 (2.3)	0.15
Alcohol	2.2 (3.0)	3.7 (4.3)	0.03
Coffee	6.5 (5.1)	7.7 (6.8)	0.27
Tea	1.9 (2.5)	2.1 (3.6)	0.68

In 2884 front-line healthcare workers from six countries (France, Germany, Italy, Spain, UK, USA)

Individuals on plant-based diets higher in vegetables, legumes and nuts, and lower in poultry and red and processed meats, had 73% lower odds of moderate-to-severe COVID-19



Kim et al BMJ NPH 2021

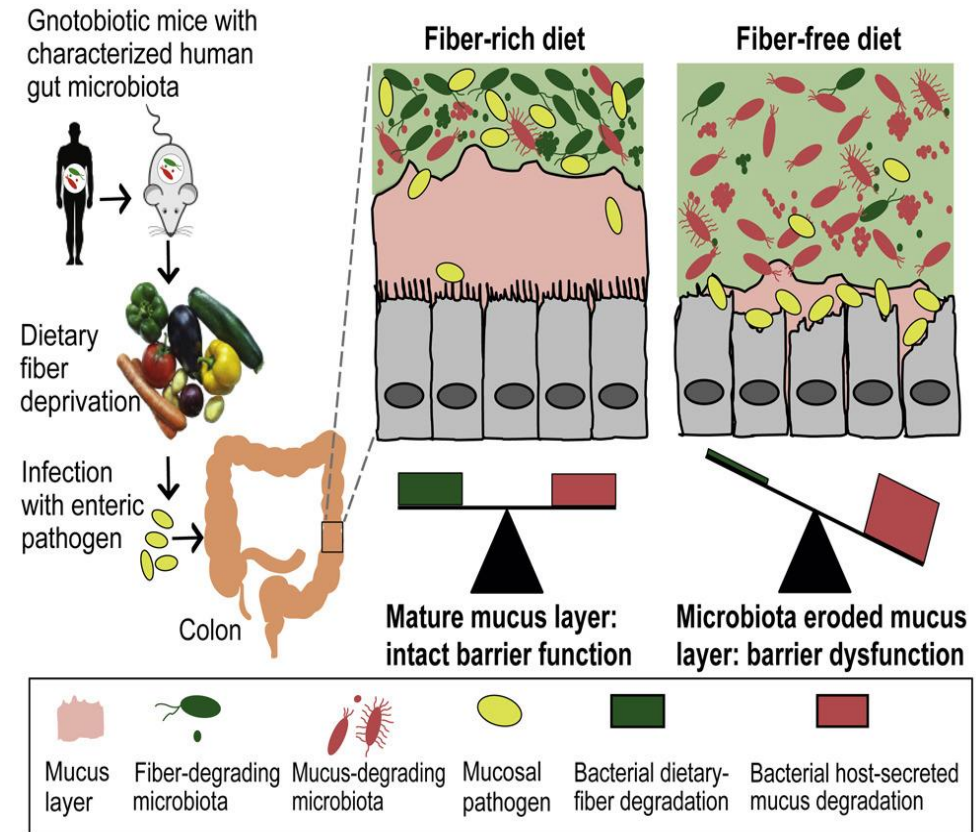
The Fiber Gap

Recommended Daily Intake:
30 grams from food sources (only plants)

THE FIBER GAP

67% consumers believe
they meet their fiber needs
(International Food Information Council)

In reality, only 5% do so!
(2009-2010 NHANES survey data)



Dietary changes after a cancer diagnosis

421 patients with plasma cell disorders surveyed via HealthTree Foundation

Since your diagnosis, have you had questions about diet and nutrition? 82%

Oncologist did not address it 57%

If your oncologist gave you recommendations, did you attempt to follow them? 94%

Patients' self reported (pre versus post diagnosis) –

- Increase in fruits, vegetables, whole grains, plant proteins, seafood consumption ($p < 0.0001$)
- Decrease in red meat and junk food consumption ($p < 0.0001$)



Malik M et al. Blood Cancer J 2022

World Cancer Research Fund Guidelines



Foods that Fight Cancer

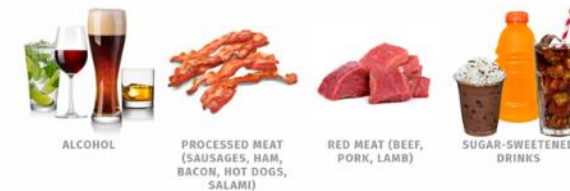
No single food can protect you against cancer by itself.

But research shows that a diet filled with a variety of vegetables, fruits, whole grains, beans and other plant foods helps lower risk for many cancers. In laboratory studies, many individual minerals, vitamins and phytochemicals demonstrate anti-cancer effects.



Foods to Limit

A lot of us grow up eating foods that might be okay to eat, but aren't necessarily the best thing to eat. As you build your meal plans, make sure you're not overdoing it with foods that are best to have in small portions.



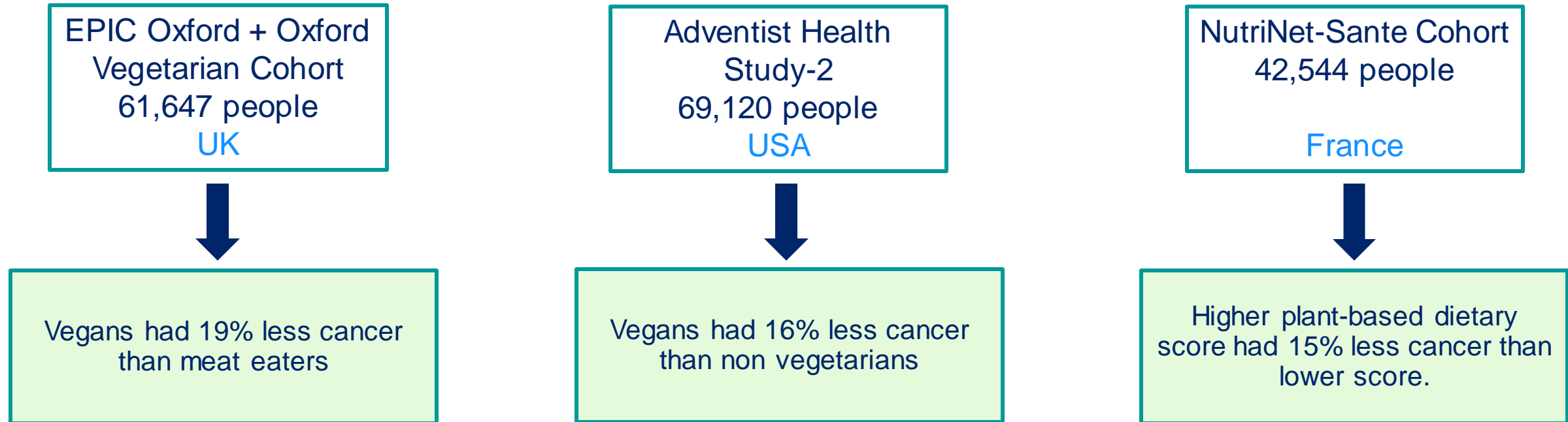
ABOUT **1/3** OF THE MOST COMMON CANCERS COULD BE **PREVENTED** THROUGH **DIET, WEIGHT AND PHYSICAL ACTIVITY**

AICR

Although ACS/AICR have published dietary guidelines, only 34% of respondents were aware of these guidelines, and of this group 47% attempted to follow them

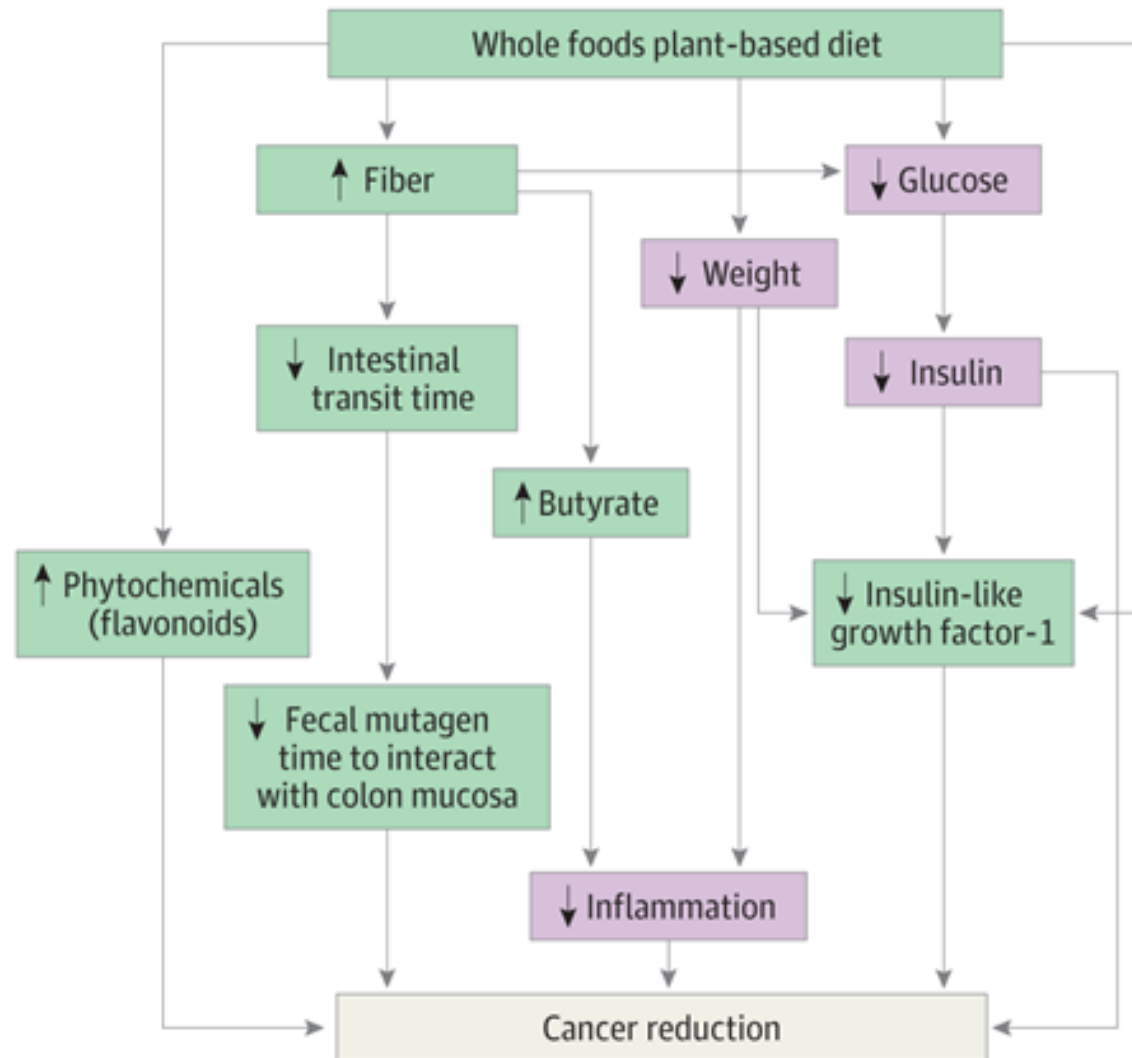
Malik M et al. Blood Cancer J 2022; <https://www.aicr.org/cancer-prevention/food-facts/>

Prediagnosis Dietary Patterns and Cancer



Key et al. Am J Clin Nutr 2014; Tantamango-Bartley et al CEBP 2013;
Kane-Diallo IJC 2018

Dietary Mechanisms



Shah UA et al. JAMA Oncology 2022 and Shah UA et al Leukemia 2023

Rethinking Diet as a Drug with Standard Treatment?

Prevention

Dietary therapies as backbone

Reducing the risk of development of a primary or secondary cancer.

Prevent other medical problems and cancers.

Treatment

Synergy with

- Checkpoint inhibitors
- Bispecific antibodies
- CAR T cells
- Monoclonal antibodies
- Vaccines
- Immunomodulatory drugs
- Chemotherapies

Fewer comorbidities means fewer side effects and ability to give full dose treatment.

Survivorship

In combination with maintenance therapy or as single agent

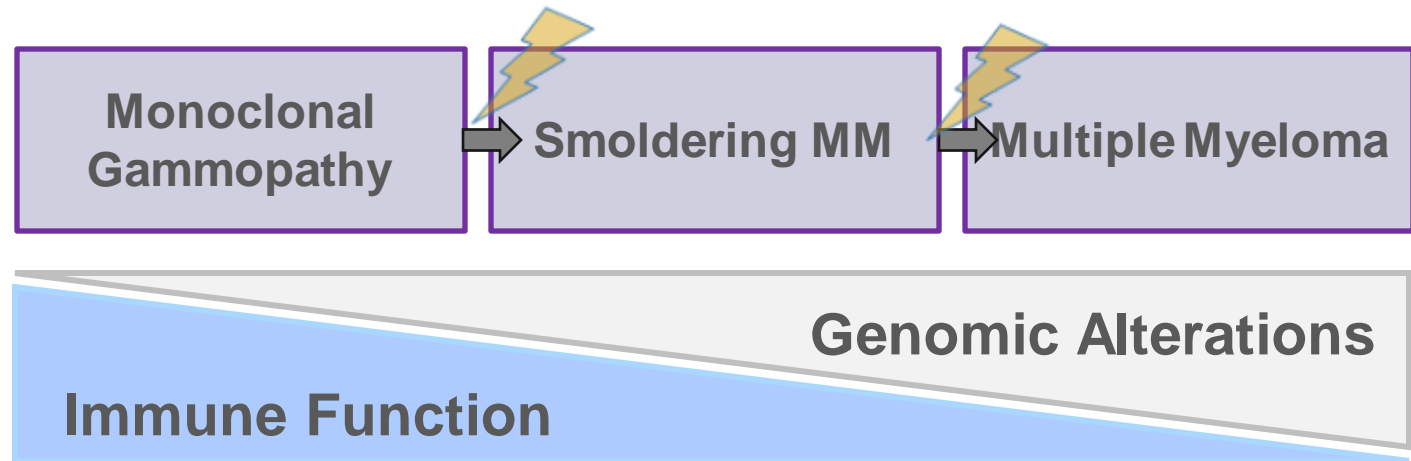
Decreasing the likelihood of a relapse once in remission.

Reduce the risk of other medical problems and cancers.

Given early detection, as hematologists and oncologists, we have an **Opportunity for Secondary Prevention**

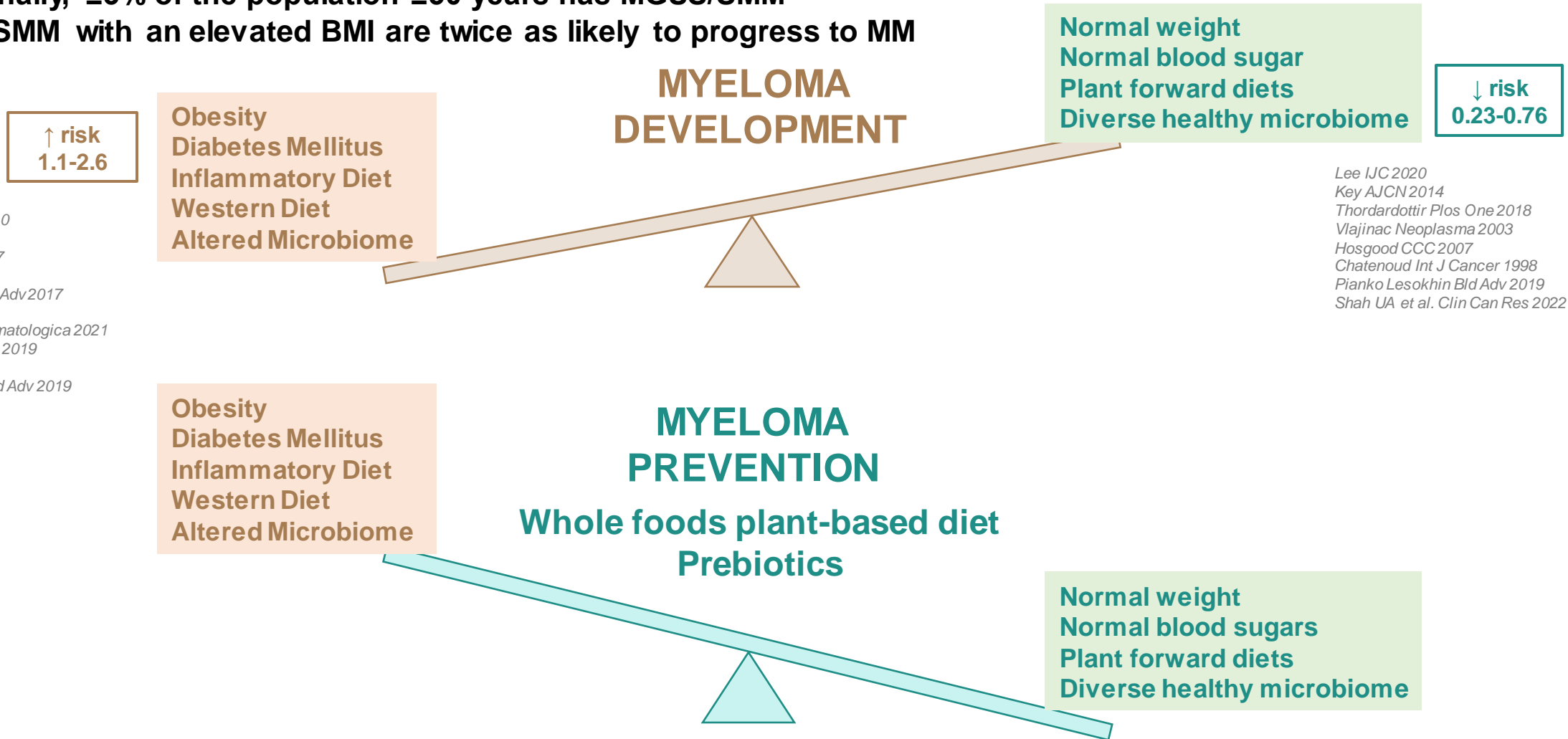
Prevention

- Dietary therapies as backbone
- Reducing the risk of development of a primary or secondary cancer.
- Prevent other medical problems and cancers.



Tilting the Scale for Myeloma Development

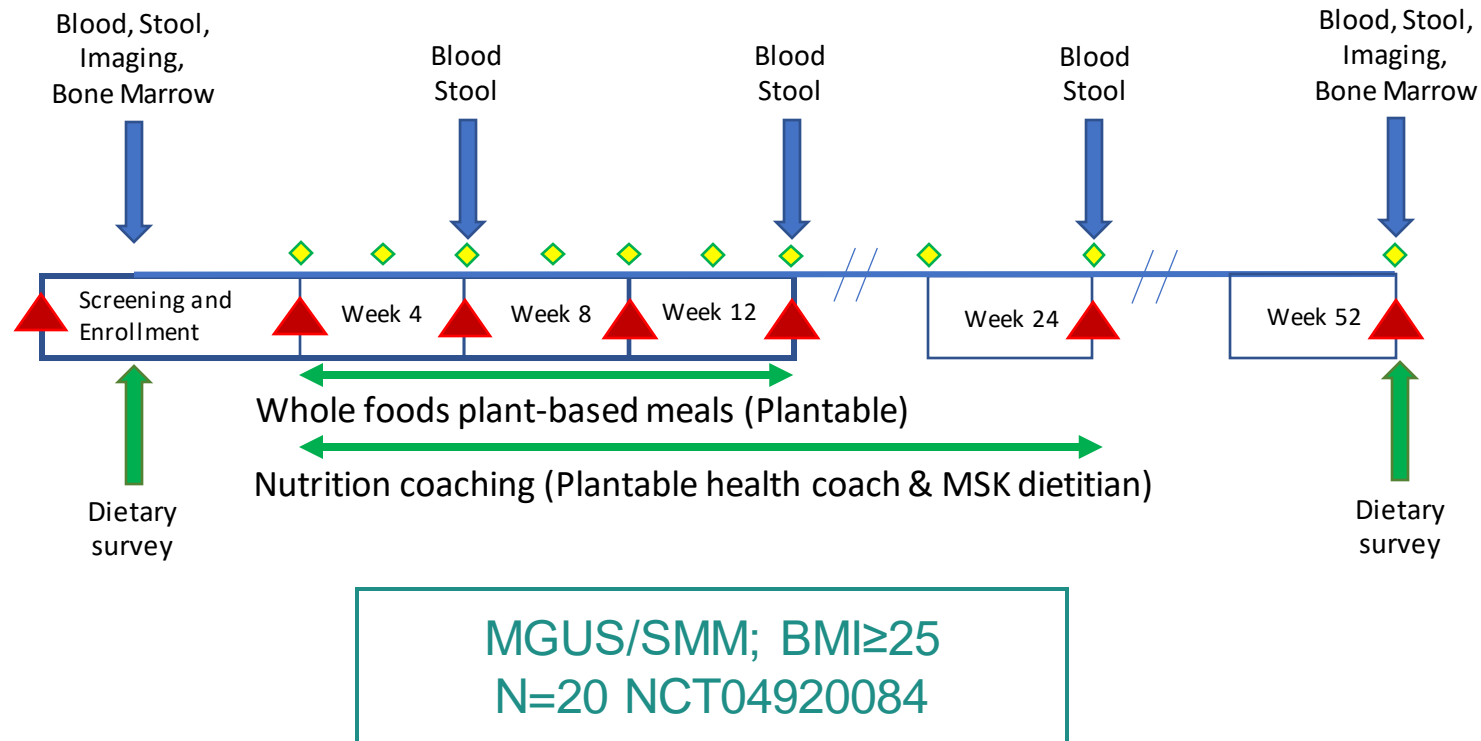
In the US population, 70% have an elevated BMI and 45% are prediabetic/diabetic
Additionally, $\geq 3\%$ of the population ≥ 50 years has MGUS/SMM
MGUS/SMM with an elevated BMI are twice as likely to progress to MM



Landgren Blood 2010
Teras BJH 2015
Birmann CEBP 2017
Chang JNCI 2017;
Thordardottir Blood Adv 2017
Dankner AJE 2015
Shah UA et al, Haematologica 2021
Lee JNCI Can Spec 2019
Lee IJC 2020
Pianko Lesokhin Bld Adv 2019

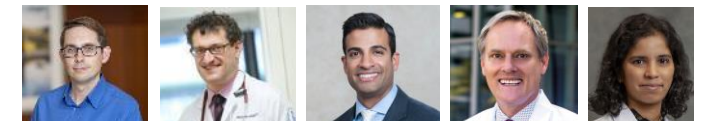
Lee IJC 2020
Key AJCN 2014
Thordardottir Plos One 2018
Vlajinac Neoplasma 2003
Hosgood CCC 2007
Chatenoud Int J Cancer 1998
Pianko Lesokhin Bld Adv 2019
Shah UA et al. Clin Can Res 2022

NUTRIVENTION Trial and Demographics



Shah UA et al. ASH 2023; IMS 2023

- 3 patients dropped out during 12-week intervention and were replaced.
- 2 patients were lost to follow up after 12 weeks and were not replaced.
- 18 patients completed 1 year on study in September 2023



Dietary Adherence and Quality of Life

- Meets feasibility endpoint (mean adherence >70% and BMI reduction >5% at 12 weeks)
- Patients were eating to satiety with no calorie restriction

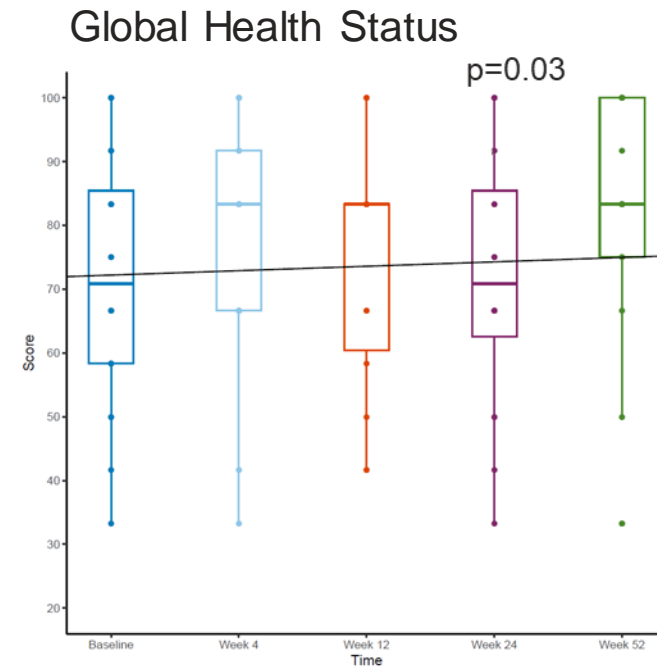
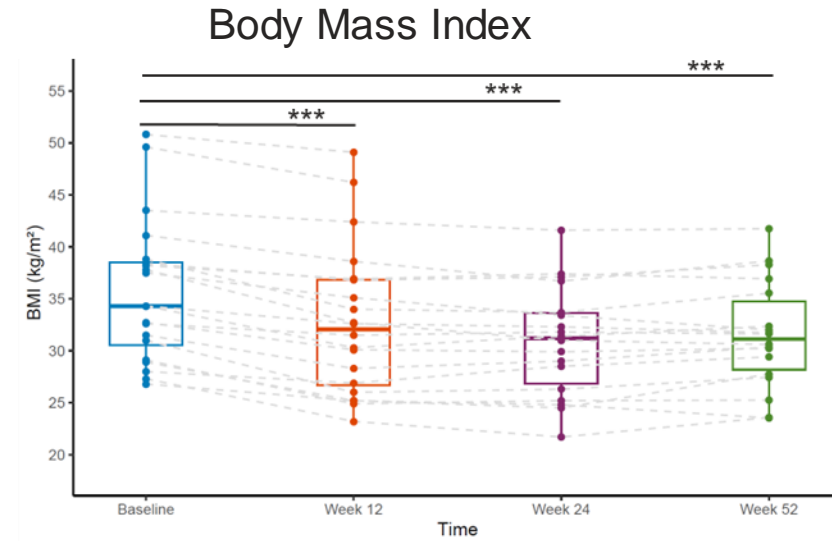
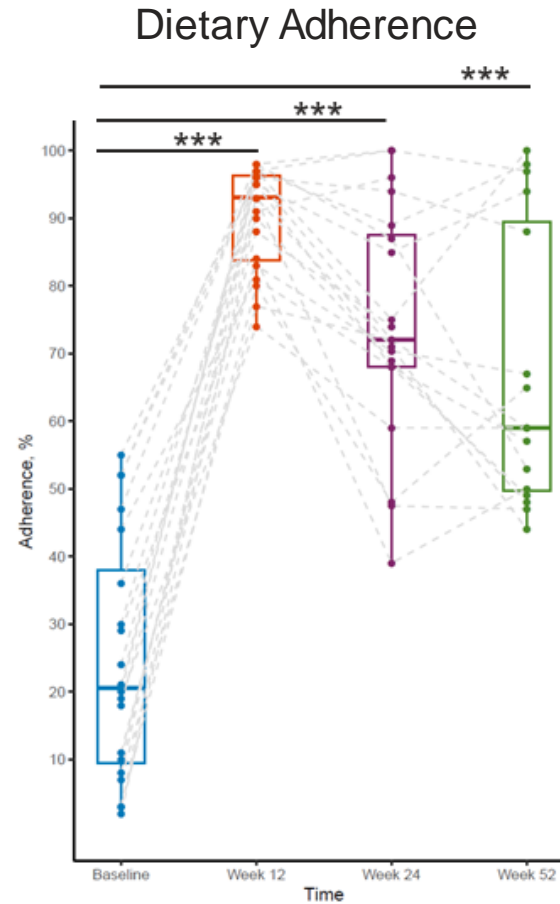
EORTC QLQ C30

A significant improvement in

- Global health status (p=0.03)
- Dyspnea (p=0.001)
- Fatigue (p=0.06)



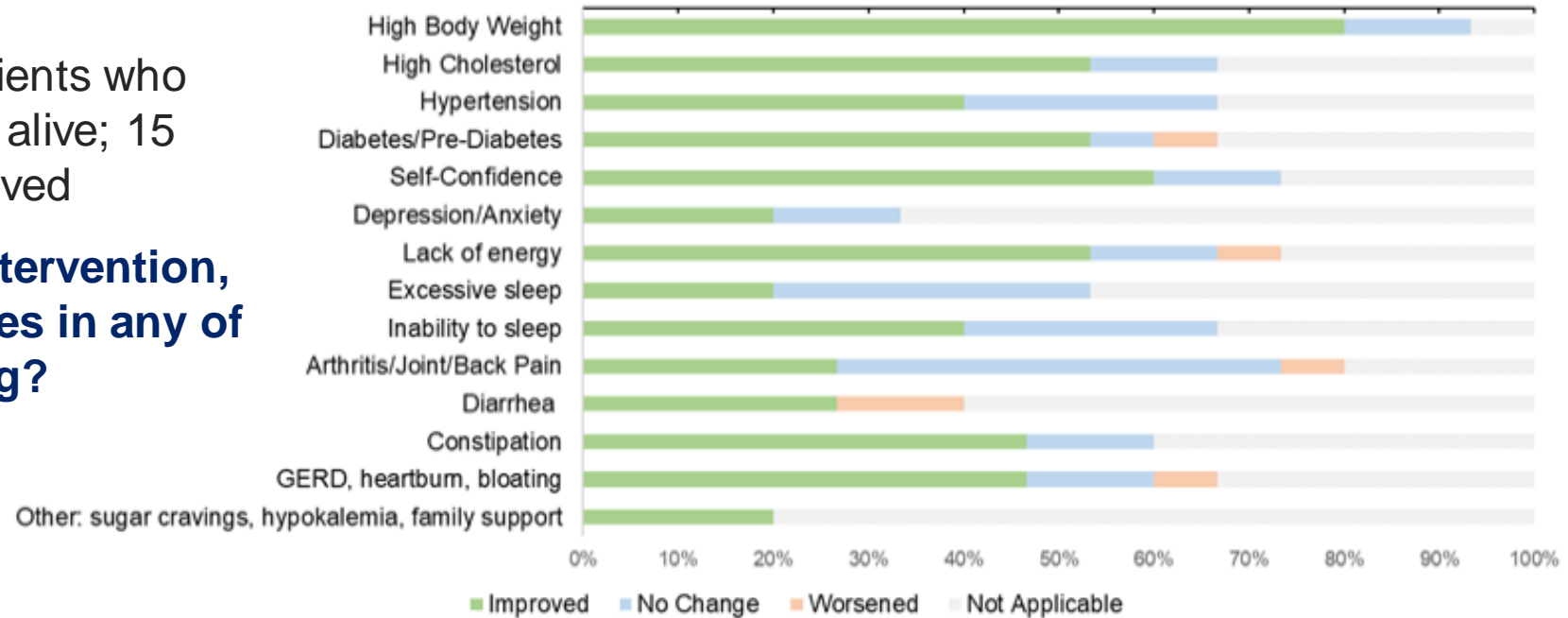
Shah UA et al ASH 2023; *IMS* 2023



Post-Intervention Survey

Survey sent to 17 patients who completed study and alive; 15 responses received

During the dietary intervention, did you notice changes in any of the following?



- **All** patients reported the intervention to be easy to follow (14 very/somewhat easy, 0 somewhat/very difficult)
- **All** patients reported they would sign up again for the intervention (14 yes, 0 no)
- 4 patients reported they were able to stop medications, **saving** an average of **\$62.50 per month** (range \$20-100)

“I was able to attain a healthy weight and have maintained the weight since starting the meals. I feel good, have energy and no bloating.”

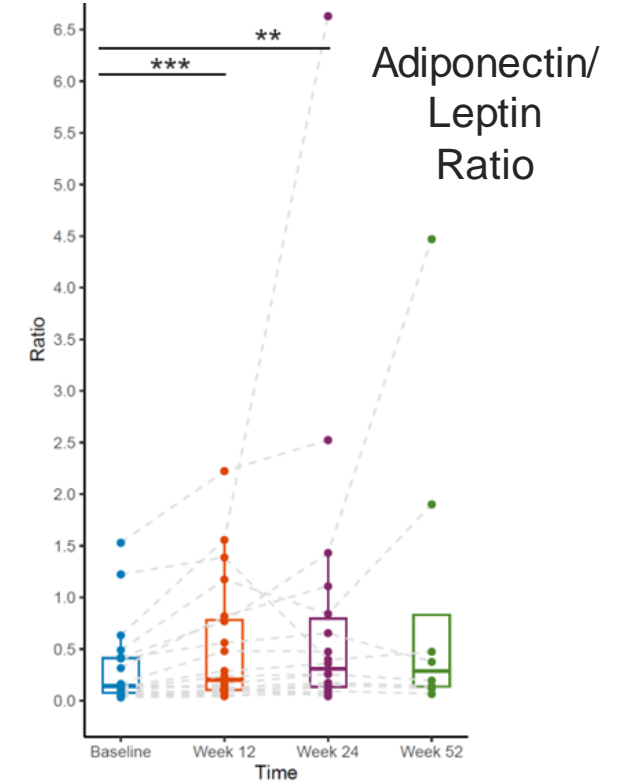
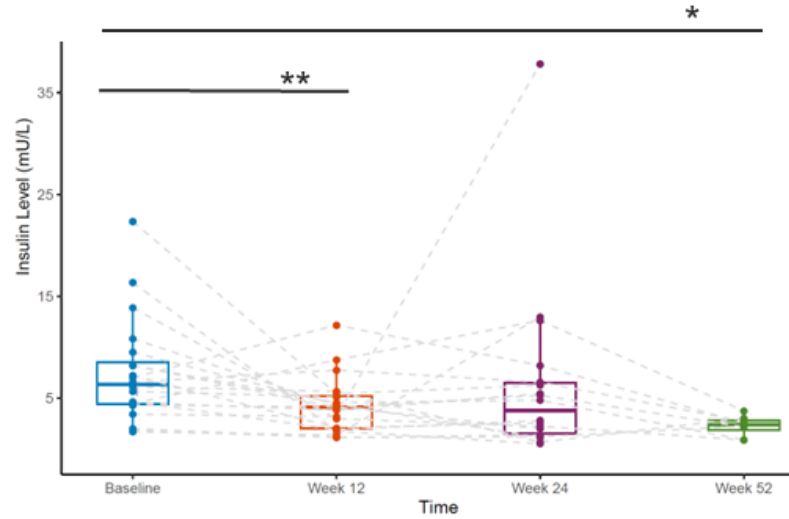
– NUTRIVENTION Patient



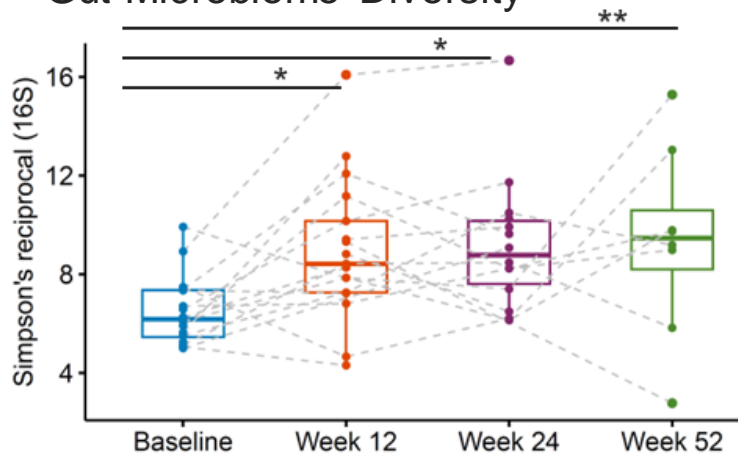
Metabolic, Microbiome and Immune Results

- Higher adiponectin leptin ratio implies less insulin resistance.
- Low adiponectin, high leptin and high insulin are associated with myeloma progression.
- Improved gut microbiome diversity and butyrate producers
- Reduced inflammation

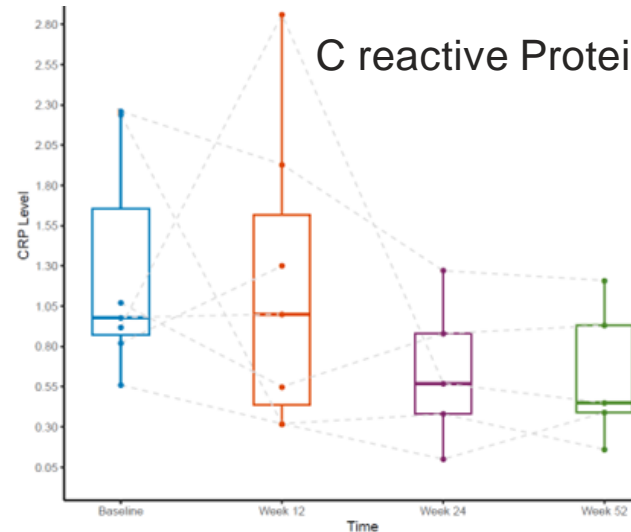
Fasting Insulin



Gut Microbiome Diversity



C reactive Protein



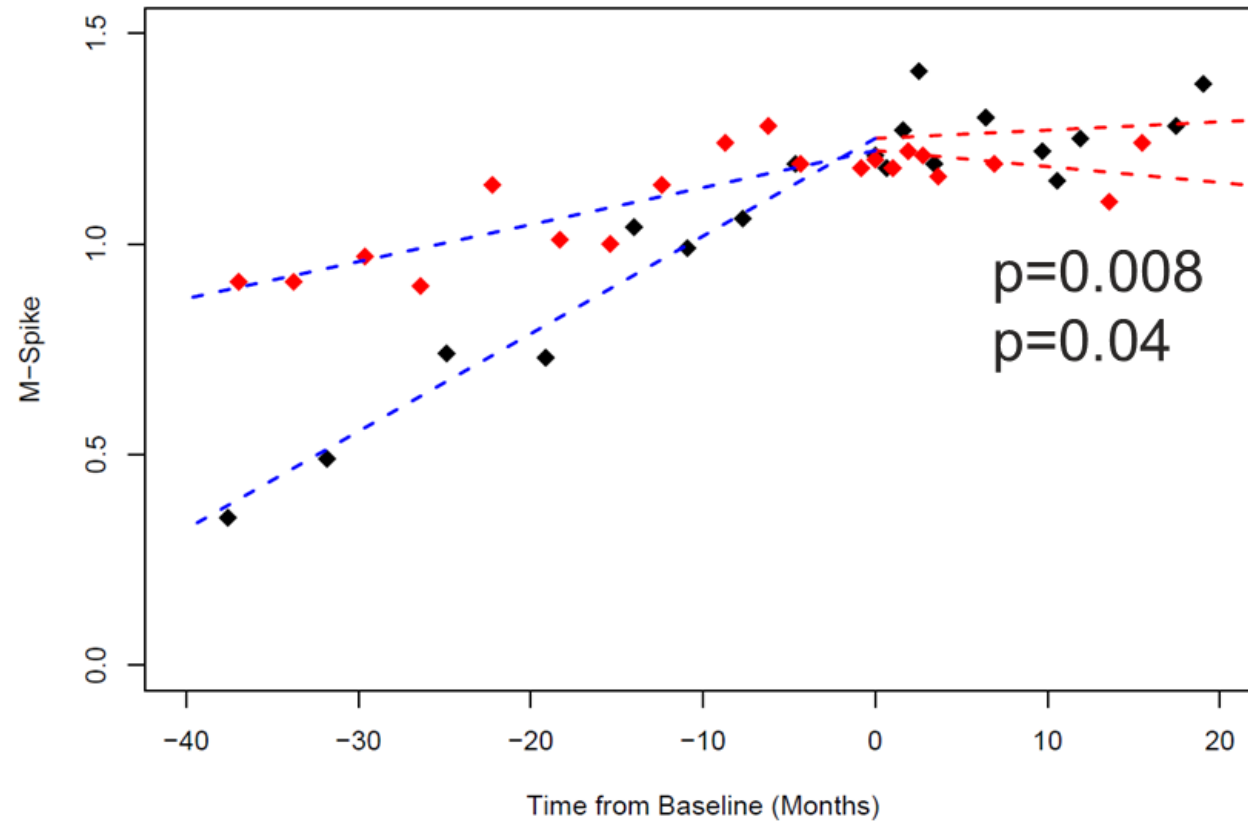
Shah UA et al. ASH 2023 and IMS 2023; unpublished data

© 2023 Memorial Sloan Kettering Cancer Center, et al. All rights reserved.

Two patients on the study

71-yo M (Mayo Int Risk IgGκ/IgGλ MGUS)

61-yo F (IMWG Int Risk IgGκ SMM)



Shah UA et al. ASH 2023

“It looked pretty dark back in 2010. Thanks to this trial, I’m into the light.”

NUTRIVENTION trial

Before NUTRIVENTION



After NUTRIVENTION



<https://www.mskcc.org/msk-news/summer-2023/food-as-medicine-why-one-doctor-thinks-diet-could-help-control> (with patient permission)

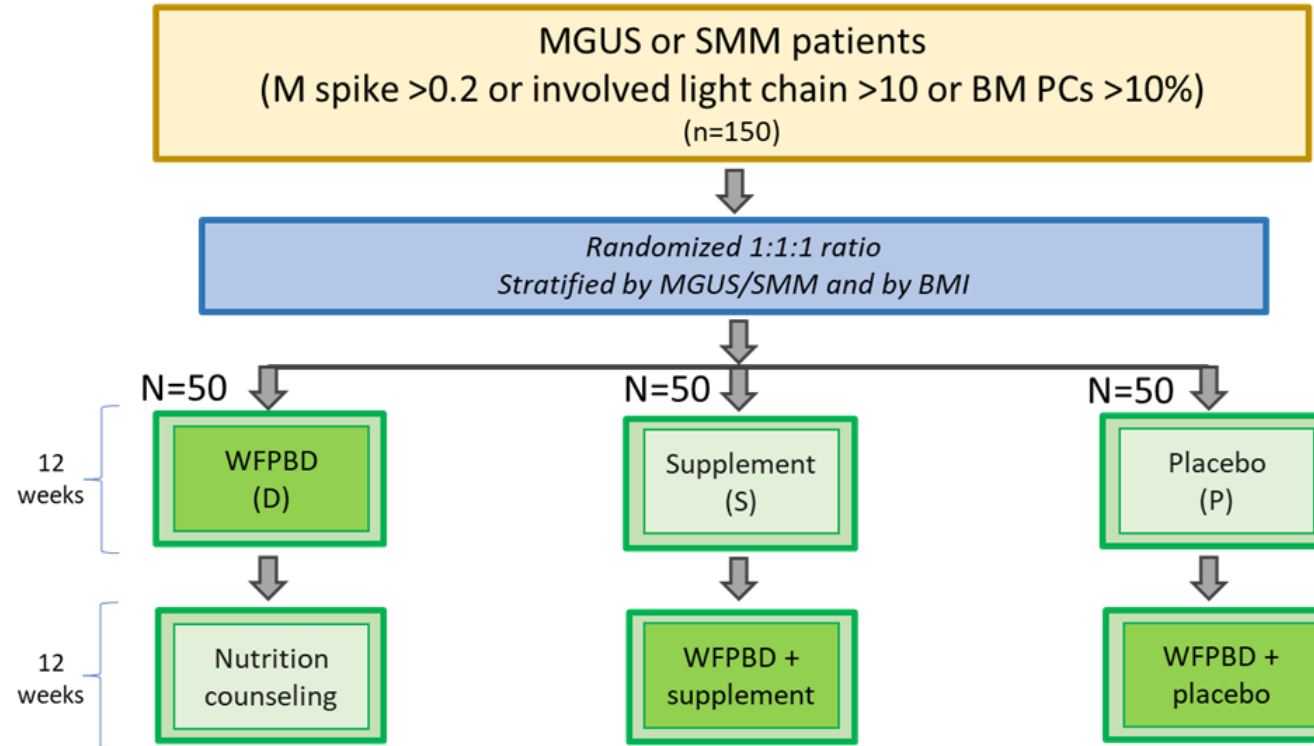
NUTRIVENTION-3 Trial is Enrolling

Q: Impact of dietary vs supplementary vs placebo interventions on the microbiome especially butyrate producers in MGUS and SMM patients

MGUS/SMM
N=150
NCT05640843

Currently enrolling at MSK in NYC

Participant needs 6 visits to MSK spread over 12 months of the trial once enrolled.



Dietary supplements: Algae omega-3 from VeggieDoctor and M and M labs, curcumin with bioperine from Sabinsa Pharmaceuticals
WFPBD: whole foods plant-based diet - Meals provided with nutrition counseling from Plantable



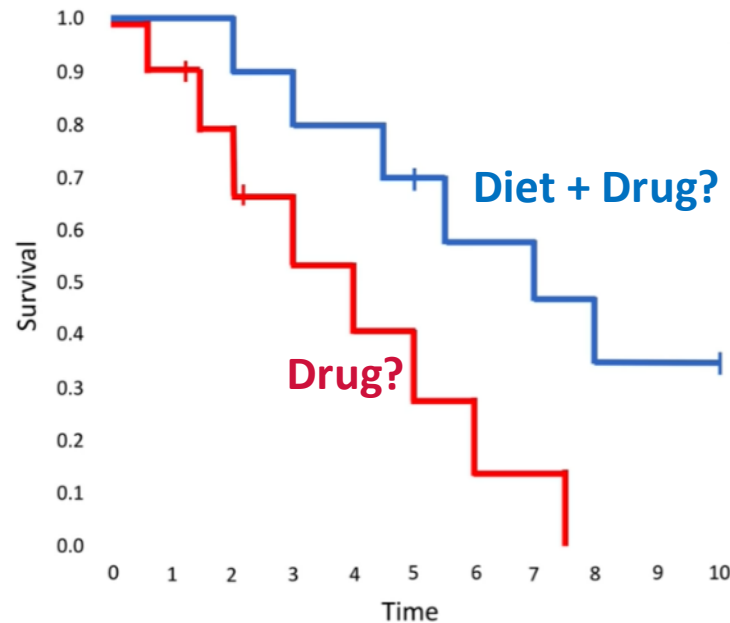
Dietary Synergism with Conventional Therapies

Treatment

Synergy with

- Checkpoint inhibitors
- Bispecific antibodies
- CAR T cells
- Monoclonal antibodies
- Vaccines
- Immunomodulatory drugs
- Chemotherapies

Fewer comorbidities means fewer side effects and ability to give full dose treatment.



Additive or synergistic activity of diet with standard of care?

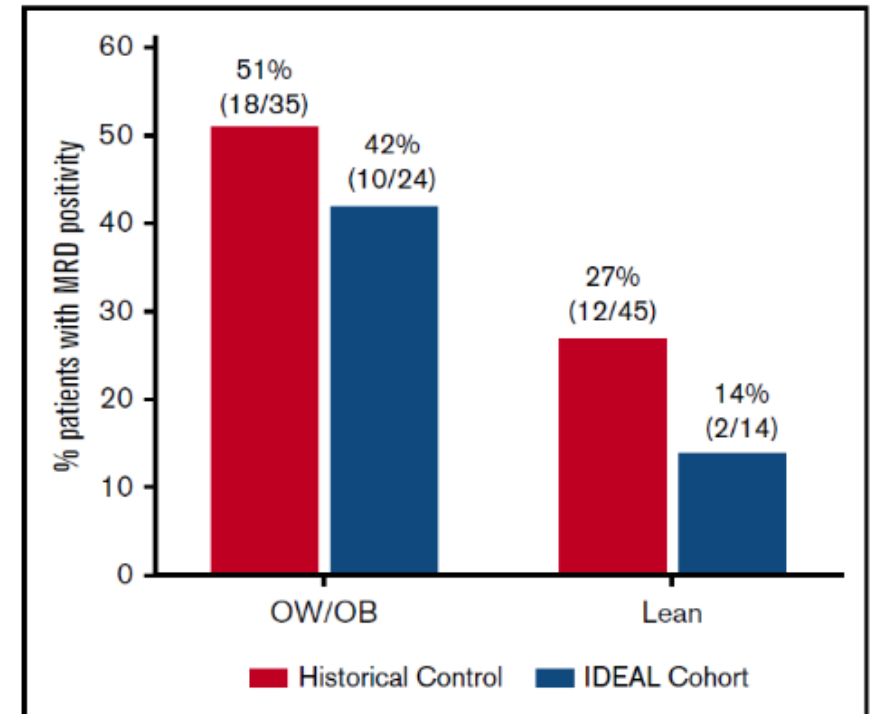
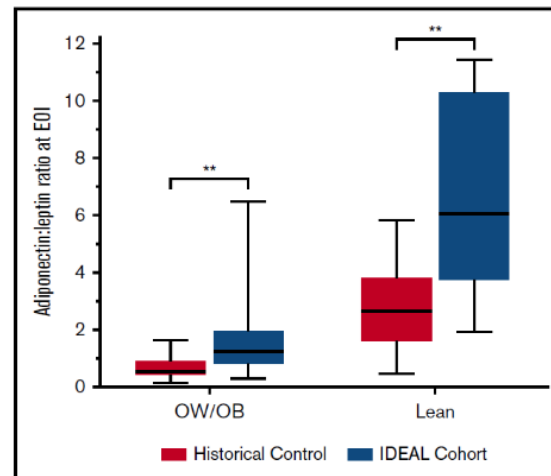
Improved

- MRD Negativity?
- PFS?
- OS?
- Quality of Life?

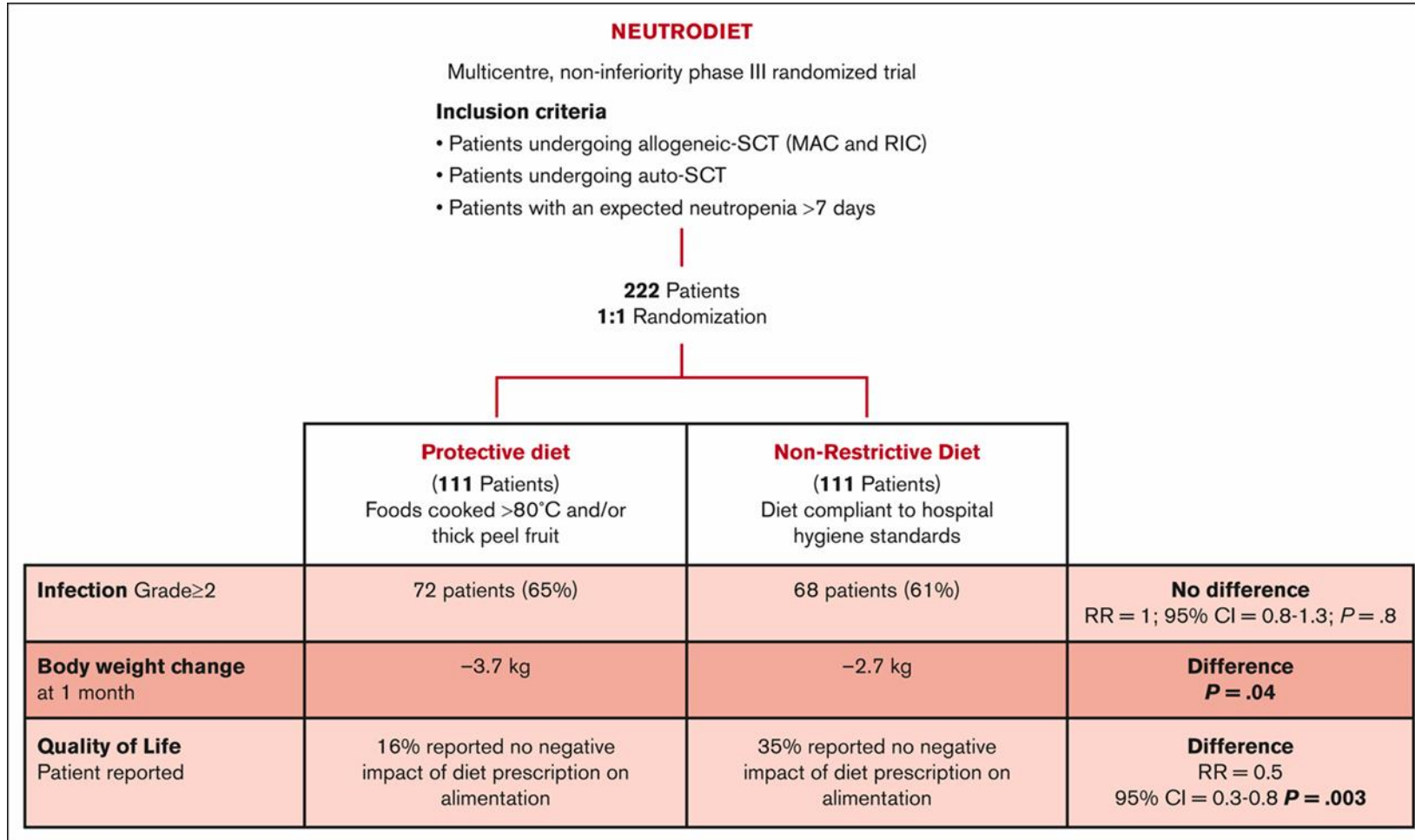
IDEAL Trial in High-Risk Acute Lymphoblastic Leukemia

- 40 patients
- Newly diagnosed
- Prospective, nonrandomized, single arm study compared to historical control
- 20% caloric deficit - 10% reduced calorie intake and 10% increased exercise
- USDA MyPlate and Traffic Light
- 28 days during cycle 1
- Primary endpoint: % change in fat mass during induction
- NCT02708108

Orgel et al. *Bld Adv* 2021

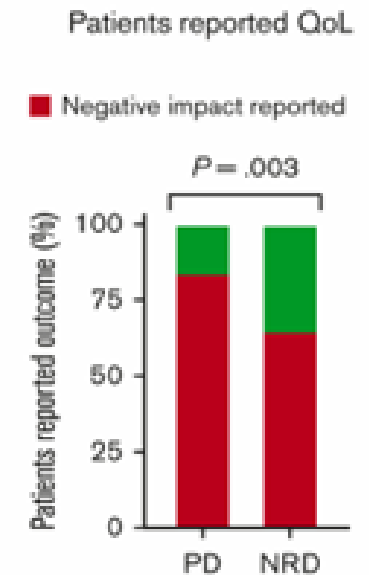
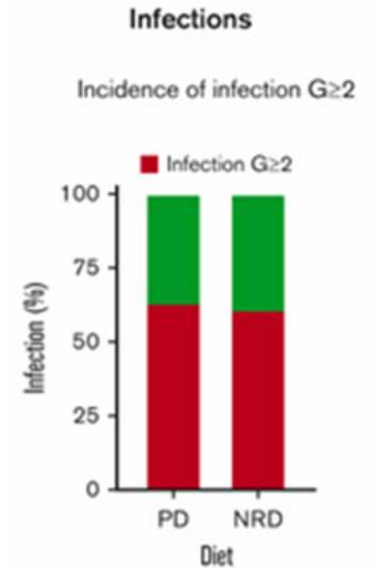


Neutro-Diet Trial

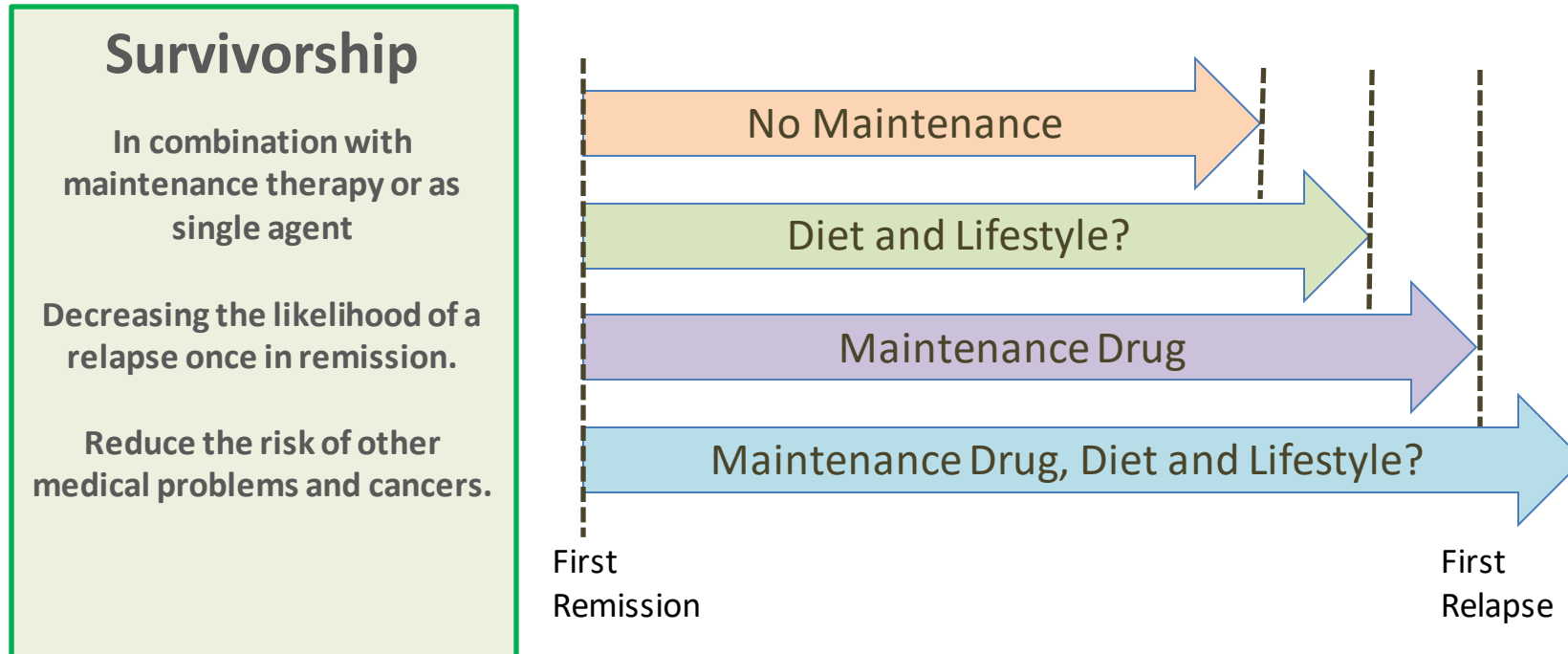


Non-Restrictive Diet allowed fresh fruit and vegetables

Stella et al. Bld Adv 2023



Dietary Interventions to Improve Survival

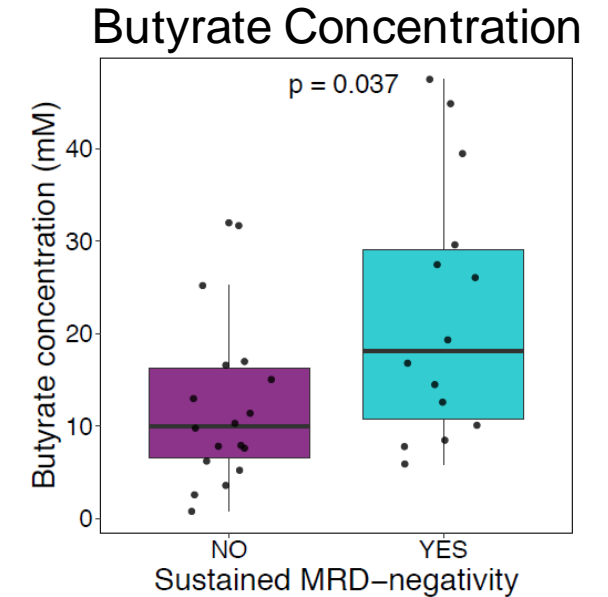
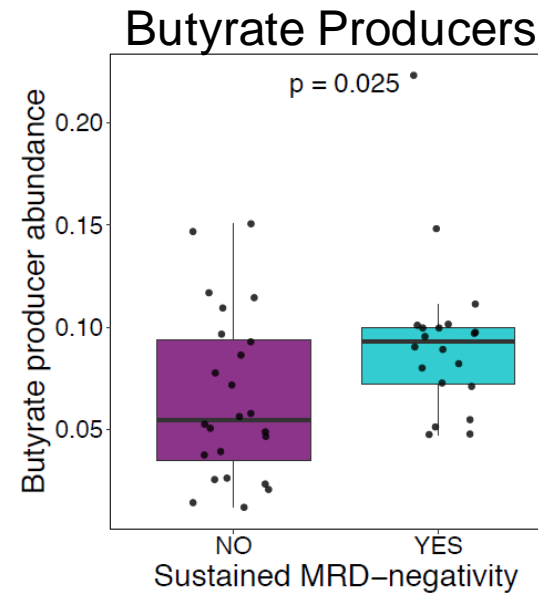
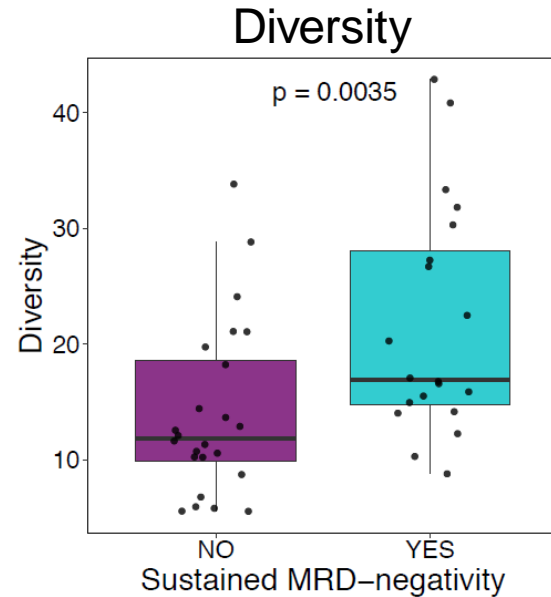


Diet & Microbiome Correlate with Sustained MRD Negativity

Clinical trial at MSK

MM on Lenalidomide
Maintenance therapy

Lenalidomide 10 mg 21/28
days for 5 years

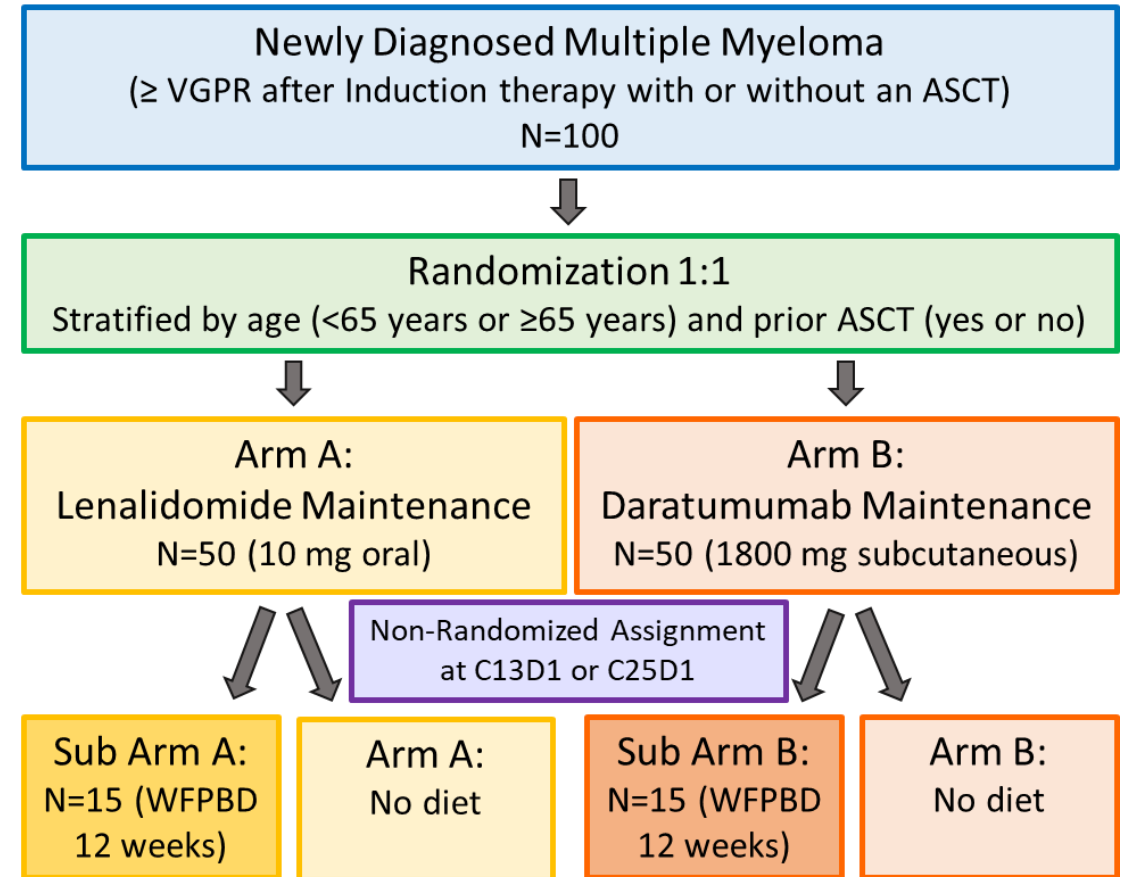
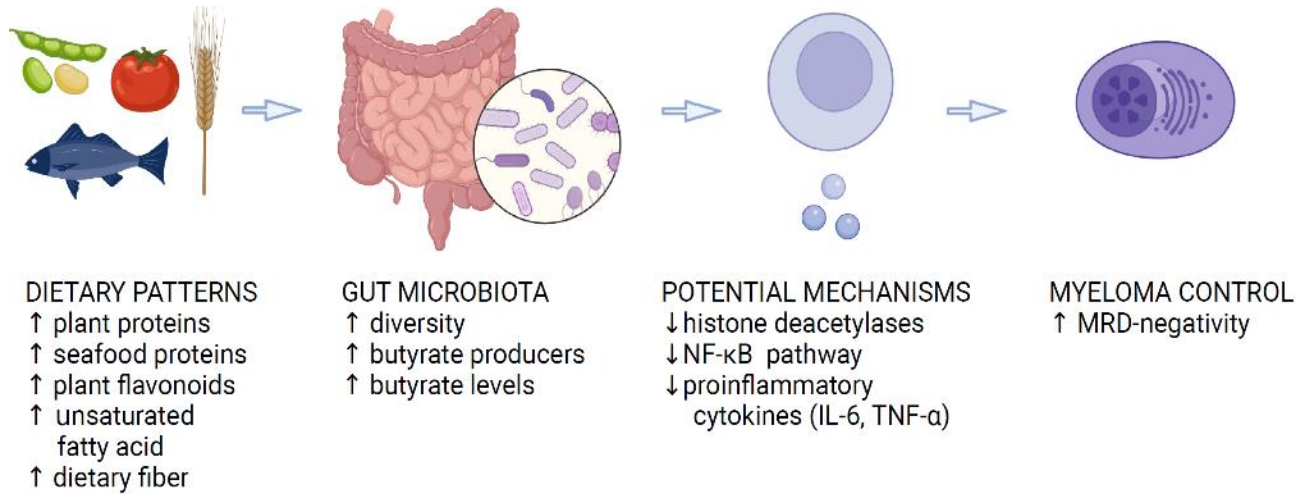


Healthy Eating Index 2015	Butyrate level at 3m		Sustained MRD-negativity
	R	p-value	p-value
Total Protein	0.5	0.004	0.02
Seafood and Plant Protein	0.45	0.009	0.02

Total Dietary Flavonoids	Butyrate level at 3m	
	R	p-value
Total anthocyanidins	0.47	0.01
Total flavones	0.48	0.01
Total flavanols	0.42	0.02
Dietary Flavonoid Diversity Index	0.46	0.008

Shah UA et al. Clin Can Res 2022

Hypothesis and Mechanisms for this Correlation



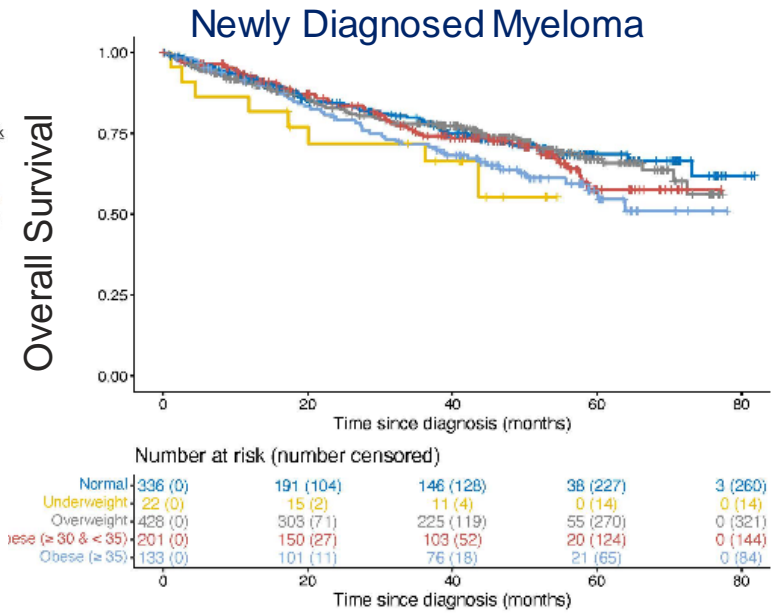
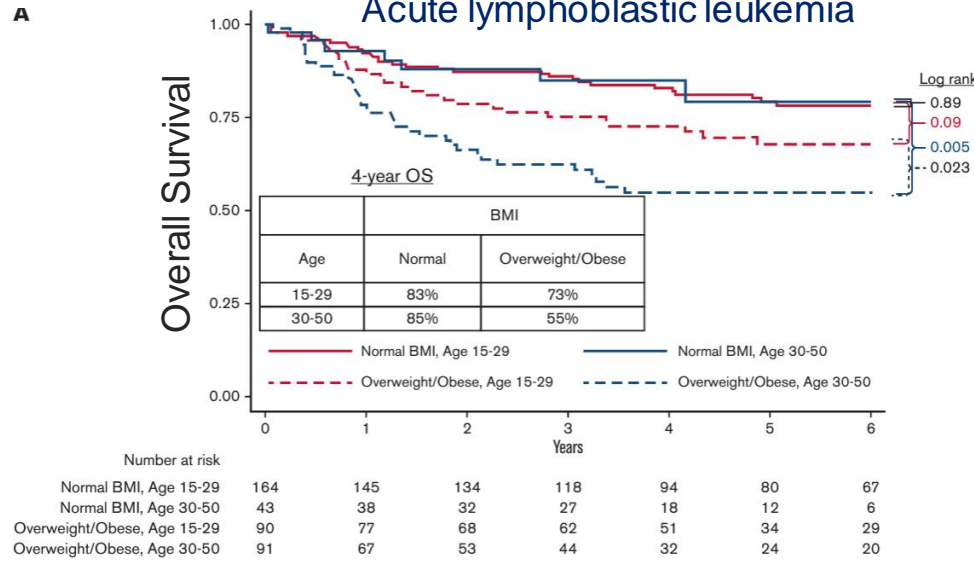
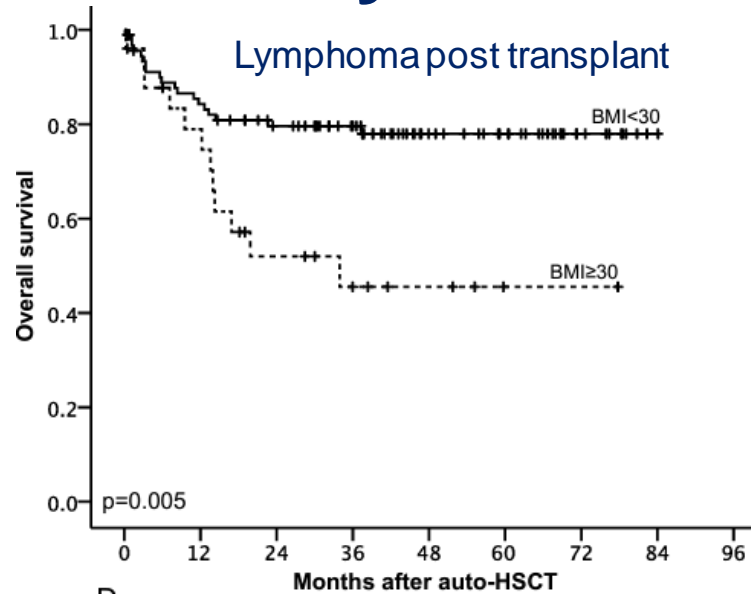
WFPBD: Whole foods plant-based diet and nutrition coaching from Plantable

Shah UA et al. Clin Can Res 2022

Enrolling at MSK (NYC) - NCT04497961

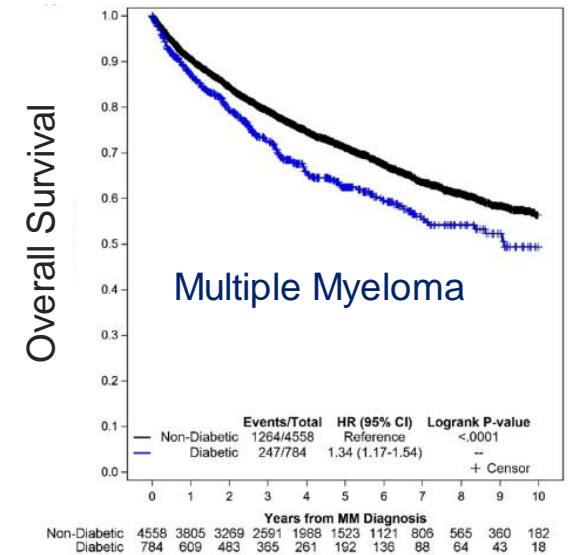
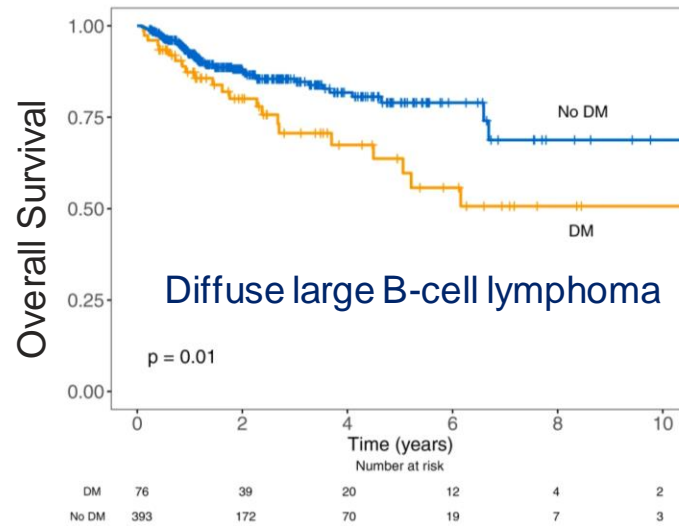
Primary Endpoint: Quality of Life

Obesity on Survival



Diabetes on Survival

Scheich et al. PLOS One 2019; Shimony et al. Bld Adv 2023; Shah UA et al. Blood Cancer J 2023; Shah UA et al. Blood Advances 2023; Drozd-Sokolowska et al. Sci Rep 2020



Fiber Requirements (example)

Recommended daily intake = 30 grams
(Males = 38 grams;
Females = 25 grams)

Fiber	Western diet	High fiber diet
Breakfast	1 egg = 0g 3 strips bacon = 0g 1 slice wheat bread = 1g	1 cup cooked oatmeal = 4g 1 tbsp peanut butter = 1g
Lunch	Small chicken breast = 0g 1 bag frozen broccoli = 12g	1 bag frozen broccoli = 12g 1 cup lentils = 16g 1 cup brown rice = 4g
Dinner	Beef 1 serving = 0g 1 cup white rice = 1g 1 baked potato = 3g	1 cup black beans = 15g 1 medium ear corn = 2g 1 avocado = 9g
Snack	1 cup yogurt = 0g 1 slice cheese = 0g	1/4 cup almonds = 5g 1 banana = 3g
TOTAL fiber	17g	71g

Protein Requirements (example)

Recommended daily intake
= 0.8-1.2 g/kg
60 kg person
= 48-72 grams

Protein	Western diet	High fiber diet
Breakfast	1 egg = 6g 3 strips bacon = 12g 1 slice wheat bread = 3g	1 cup cooked oatmeal = 6g 1 tbsp peanut butter = 4g
Lunch	Small chicken breast = 23g 1 bag frozen broccoli = 7g	1 bag frozen broccoli = 7g 1 cup lentils = 18g 1 cup brown rice = 4g
Dinner	Beef 1 serving = 34g 1 cup white rice = 4g 1 baked potato = 4g	1 cup black beans = 15g 1 corn on the cob = 5g 1 avocado = 3g
Snack	1 cup yogurt = 9g 1 slice cheese = 4g	1/4 cup almonds = 8g 1 banana = 1.5g
TOTAL protein	106g	72g

Discussing Nutrition Must Be Individualized

- Disease Stage – Newly diagnosed, on maintenance, relapsed
- Patient Choice – Receptive to hearing about this and empowered by it or overwhelmed and would not help
- Medical issues related to the cancer – Do they have significant weight loss from their cancer and side effects to treatment like nausea and diarrhea that they aren't tolerating most foods.
- Medical issues related to metabolic health – Obesity, diabetes, cardiovascular disease, high cholesterol
- Gradual versus drastic changes to habits

Some Practical Dietary Tips to Consider Incorporating

Carbohydrates – ↑ whole, unrefined

- ↑ Whole grains (>3 servings/day)
- ↓ Unprocessed/refined carbs/foods
- ↓↓ Sugary foods/drinks

Fiber (↑ >30 grams/day)

- ↑ Fruits/Vegetables (>5-6 servings/day)
- ↑ Diversity of plant foods (>30 types/week)

Protein - Plant >> Animal sources

- ↑ Beans/Tofu/Tempeh
- ↓ Red/processed meats

Fermented Foods: ↑ ↑

Fats – ↑ Unsaturated fats

- ↑ Nuts/Seeds, fish, olive oil, avocados
- ↓ Fried foods
- ↓ Dairy/Cheese
- Regular omega 3 fatty acids
- Vitamin D (>30 ng/mL)

- Calorie counting/restriction are difficult to sustain long term
- Meal planning and preparation in advance
- Regular mealtimes not waiting until one is starving
- Ensure adequate hydration
- Learning to read ingredient lists and nutrition labels
- Gradual changes are more sustainable
- Making healthy swaps
- Make it a lifestyle and not a diet
- Frozen fruits/vegetable bags are healthy
- Doesn't have to be raw salads. Cooked foods healthy too

Food Labels

Honey Toasted Pecans

Nutrition Facts	
Serving size	1 ounce (30g)
Amount Per Serving	
Calories	150
% Daily Value*	
Total Fat 9g	12%
Saturated Fat 1g	5%
<i>Trans</i> Fat 0g	
Cholesterol 0mg	0%
Sodium 95mg	4%
Total Carbohydrate 19g	7%
Dietary Fiber 1g	4%
Total Sugars 18g	
Includes 18g Added Sugars	36%
Protein 1g	2%
Vitamin D 0mcg	0%
Calcium 9mg	0%
Iron 0mg	0%
Potassium 48mg	2%

*The % Daily Value (DV) tells you how much a nutrient in a serving of food contributes to a daily diet. 2,000 calories a day is used for general nutrition advice.

Eating healthy doesn't have to be boring!

It doesn't have to be salads and raw vegetables and fruits alone.

American College of Lifestyle Medicine



Goals (Pick at least one to begin)

- 1 cup beans (plant protein) daily
- 2 cups fruit daily
- 1 serving fermented food daily
- 4 cups vegetables daily
- 1/3 cup nuts/seeds daily
- <6 teaspoons added sugars
- <2,300 mg salt
- >30 plant foods/week
- 1.5 cups whole grains daily
- >75% of your plate will be plant-based foods



Conclusions

Let's change our focus in cancer from
Living Longer to

Living Better and Longer

By incorporating lifestyle changes

- Better Nutrition
- Improved Fitness

To reduce comorbidities and improve quality of life.

Acknowledgements

MSK Myeloma/BMT Faculty

Alexander Lesokhin, MD
Marcel van den Brink, MD, PhD
Saad Z Usmani, MD
 Sergio Giralt, MD
 Jonathan Peled, MD, PhD
 Sham Mailankody, MD
 Neha Korde, MD
 Hani Hassoun, MD
 Malin Hultcrantz, MD, PhD
 Carlyn Tan, MD
 Gunjan Shah, MD
 David Chung, MD
 Oscar Lahoud, MD
 Heather Landau, MD
 Michael Scordo, MD
 Kylee McLachlan, MD, PhD

Biostatistician

Andriy Derkach, PhD
 Teng Fei, PhD

Research Dietitian

Francesca Castro, RD

Research RN

Jenna Blaslov, RN

Research Associate

Jeannen Santos

Research Manager

Laura Guttentag

Fellows/Residents/Post docs

Richa Parekh, MD
 Janine Joseph, MS (Moysich lab)
 Juan Jose Garces, PhD
 Ross Firestone, MD
 Laura Cogrossi, PhD (Bellone lab)

Collaborators

Matteo Bellone, MD (Italy)
Neil Iyengar, MD (MSK)
 Ola Landgren, MD, PhD (UofMiami)
 Anita D'Souza, MD (U of Wisconsin)
 Jun Mao, MD (MSK)
 Kinga Hosszu, PhD (SKI)
 Justin Cross, PhD (SKI)
 Michael Pollak, MD (McGill U)
 Susan Chimonas, PhD (MSK)
 Jens Hillengass, MD (Roswell Park)
 Samir Parekh, MD (Mount Sinai)
 Emily Gallagher, MD (Mount Sinai)
 Catherine Marinac, PhD (DFCI)
 Susan Dewolf, MD (MSK)
 Francesco Maura, MD (UofMiami)

Patients with plasma cell disorders

 @UrviShahMD
<https://linktr.ee/urvishahmd>



NCI K12 Paul Calabresi Career Development Award
 American Society of Hematology Scholar Award
 International Myeloma Society Career Development Award

ALLEN FOUNDATION, INC.





Questions?



Urvi A. Shah MD

Assistant Attending Physician,
Myeloma Service, Memorial Sloan
Kettering Cancer Center

Let Us Know How We Can Help You



Visit our website: bmtinfonet.org

Email us: help@bmtinfonet.org

Phone: 888-597-7674 or 847-433-3313

Find us on:

Facebook, facebook.com/bmtinfonet

X, twitter.com/BMTInfoNet