MPN, Healthy Eating & the gut microbiome

MPN Symposium – University of Western Australia 6.4.18

Nathalie Cook
Accredited Practising Dietitian
MNutrDiet, BAppSc, CertPaedNutrDiet



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Healthy Eating – something we can do to stay well with MPN!

- Five food groups.
  - How much we need each day.
  - Putting it into practice!
- Diet, the gut microbiome & Inflammation.
  - *Prebiotics* – dietary fibre & resistant starch.
  - *Probiotics* – live beneficial bugs-science is still young.
- MPN NUTRIENT Study
  - Impact of diet on inflammation & MPN symptoms.
- Healthy eating tips to stay well with MPN







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Eat mostly high-fibre plant foods.

- **Vegetables: 5-6 serves/d**
- **Whole grains: 3-6 serves/d**
- **Fruit: 2 serves/d.**
- **Protein foods = ¼ plate area.**
  (lean meats, poultry, fish, tofu, nuts, & legumes/beans)
- **Dairy: 3-4 serves/d.**
  (1 serve = 250ml milk, 40g cheese, 200g yoghurt & alternatives)
- **Fish 2-3 serves/wk.**
- **Enjoy olive oil in cooking & salads.**
- **Drink plenty of water.**

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A healthy meal plate = ½ colourful veg or salad,

¼ carbohydrates (whole grains & starchy veg),
¼ lean protein (meat, chicken, fish, legumes, eggs, nuts, soy)



- 2017 CSIRO: <80% Aussies eat enough fruit & veg.
- Eat mostly plant foods for better health!

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EATFORHEALTH

FOLLOWING THE RECOMMENDATIONS IN THE AUSTRALIAN DIETARY GUIDELINES

The sample meal plan outlined below provides the nutritional and energy requirements for a WOMAN aged 19-50 years of average height, healthy weight and light activity

BREAKFAST



Wholegrain breakfast cereal with reduced fat milk

(60g cereal plus 1 cup/250mL milk)



Reduced fat yogurt

(small tub/100g)

MORNING BREAK



Coffee with milk

(200mL – small/medium size)

LUNCH



Sandwich with salad and chicken

(2 slices bread (preferably wholemeal), 40g roast chicken, 1 teaspoon margarine, 1 cup salad vegetables)



Apple

(1 medium apple)

AFTERNOON BREAK



Coffee with milk

(200mL- small/medium size)

Unsalted mixed nuts

(30g – small handful)

EVENING MEAL



Pasta with lean beef mince and red kidney beans

(1 cup of cooked pasta, 65g cooked lean beef mince / fist size scoop, ½ onion, ¼ cup kidney beans)



Green salad with olive oil and vinegar dressing

(1½ medium tomato, 2 cups green leafy salad, 2 teaspoon unsaturated oil plus vinegar to taste)

EVENING SNACK



Fruit salad (tinned or fresh) and reduced fat yoghurt

(1 cup mixed fruit plus small tub/100g yoghurt)



Drink plenty of water throughout the day

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Australian Government
National Health and Medical Research Council
Department of Health and Ageing
www.eatforhealth.gov.au

EATFORHEALTH

FOLLOWING THE RECOMMENDATIONS IN THE AUSTRALIAN DIETARY GUIDELINES

The sample meal plan outlined below provides the nutritional and energy requirements for a MAN aged 19-50 years of average height, healthy weight and light activity

BREAKFAST



Wholemeal toast with baked beans and grilled tomato

(2 slices of wholemeal bread, ½ can of baked beans, 1 medium tomato)





Glass of milk

(1 cup/250ml reduced fat milk)

MORNING BREAK



Apple

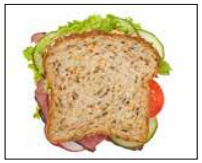
(1 medium apple)



Coffee with milk

(200mL – small/medium size)

LUNCH



Roast beef, salad and cheese sandwich

(2 x slices of wholemeal bread, 65g roast beef, 20g/1 slice reduced fat cheese, 1 cup mixed salad)

AFTERNOON BREAK



Coffee with milk

(200mL- small/medium size)

Unsalted mixed nuts

(30g – small handful)

EVENING MEAL



Grilled fish on rice with lemon juice and vegetables

(100g fillet of fish, 1 cup cooked rice, squeeze of lemon, 1 small boiled potato, ½ cup cooked zucchini, ½ cup cooked broccoli)

EVENING SNACK



Fruit salad (tinned or fresh) and reduced fat yoghurt

(1 cup mixed fruit plus small tub/100g yoghurt)





Drink plenty of water throughout the day

Microbiota & Health

- Trillions of micro-organisms live in & on us, mostly in the GI tract.
  - Bacteria, fungi, viruses >1000 species.

- Beneficial microbes (commensal) use <u>dietary fibre & resistant starch</u> as their energy source.
  - **Produce anti-inflammatory short chain fatty acids (SCFAs)**

- Harmful microbes use processed, high fat, high sugar foods.
  - **Produce pro-inflammatory metabolites.**

- Our food choices **<u>influence the balance of beneficial vs. harmful</u>** gut microbes & impact our health!



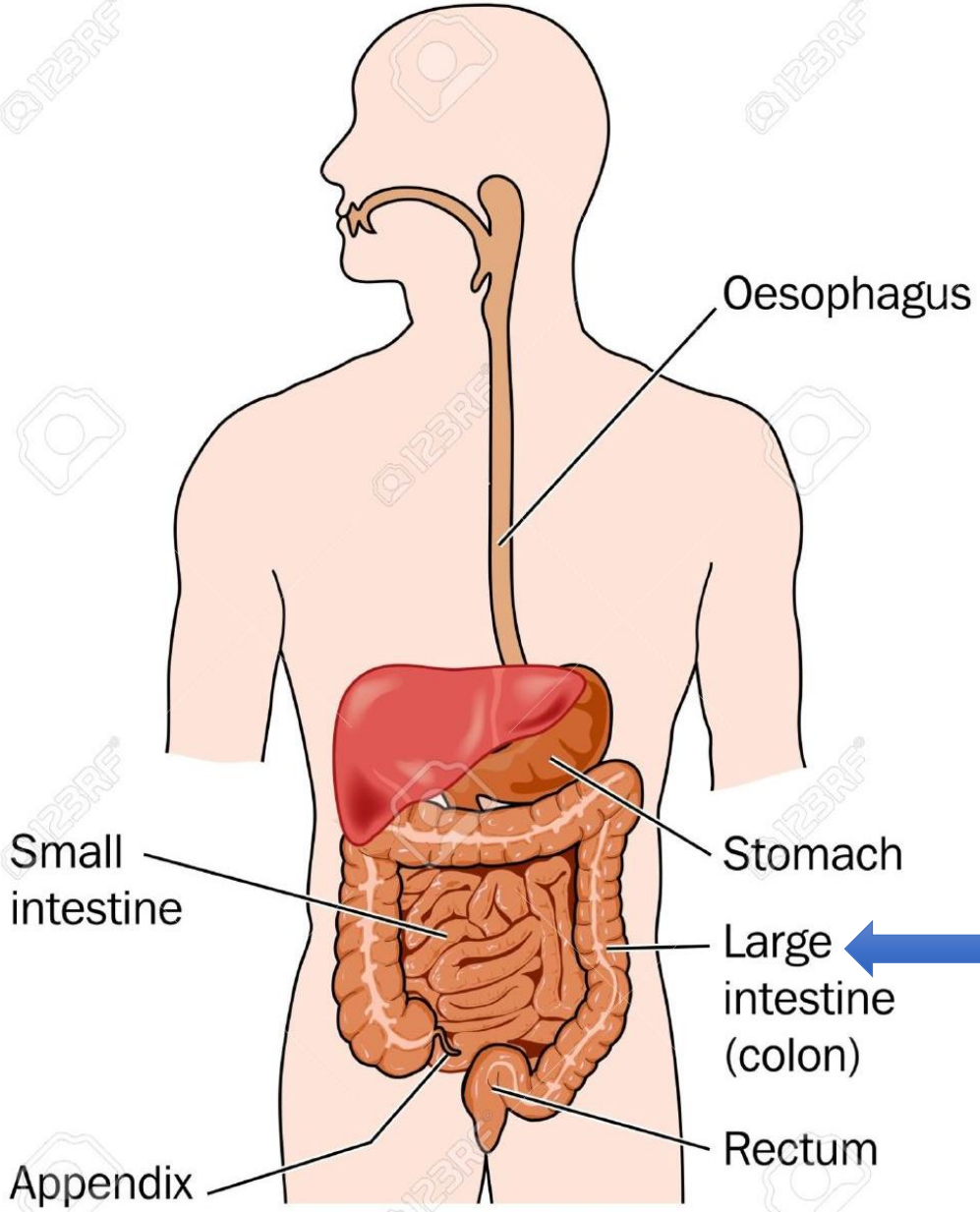
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Diet effects gut microbiota, inflammation & the immune system

- **Anti-inflammatory**- Whole grains, fruit & veg, legumes, nuts, seeds. (**high fibre/resistant starch**)
  - **Prebiotic** – feeds beneficial gut bacteria: oats, rye, barley, artichokes, onions, leeks, firm bananas, legumes, cooked & cooled rice, pasta, potatoes.
  - **Probiotic** – Live organisms: *Old practice, new science*!
    - fermented foods – yoghurt, sauerkraut, kimchi etc. Ancient methods of food preservation.
    - Probiotic supplements – Which strains? Dose? Who will benefit???
- **Pro-inflammatory**- Fast foods, soft drinks, refined carbs & sugary foods. (**low fibre/high sugar**)
- **Population who eat high fibre, plant-based diets have lower chronic disease rates.**
  - Diabetes, CVD, arthritis, inflammatory bowel disease, kidney disease etc.



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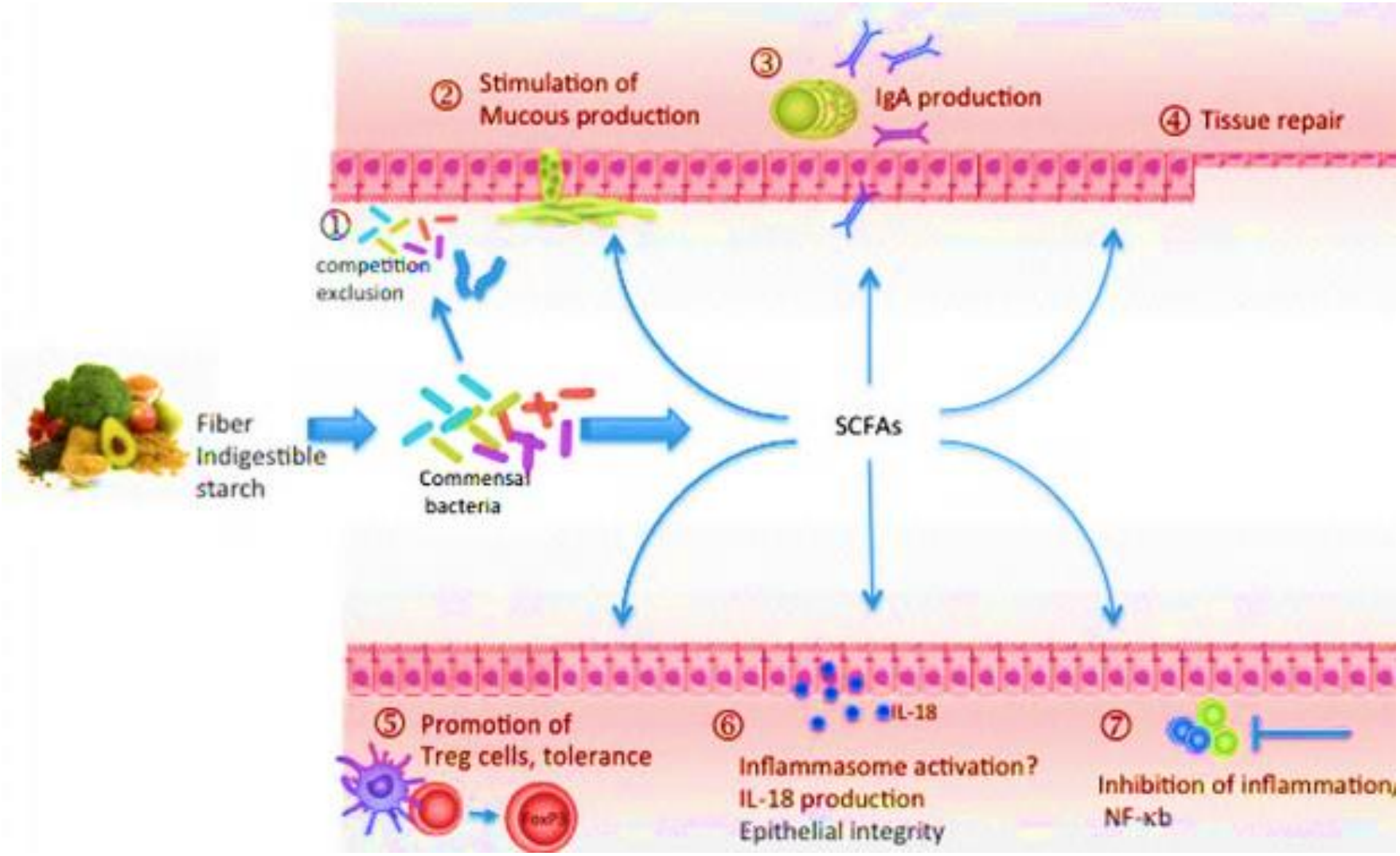
Fibre needs to get to the colon where gut flora fermented it.

Fermentation products of fibre & resistant starch (*short chain fatty acids*) **are protective & anti-inflammatory.**

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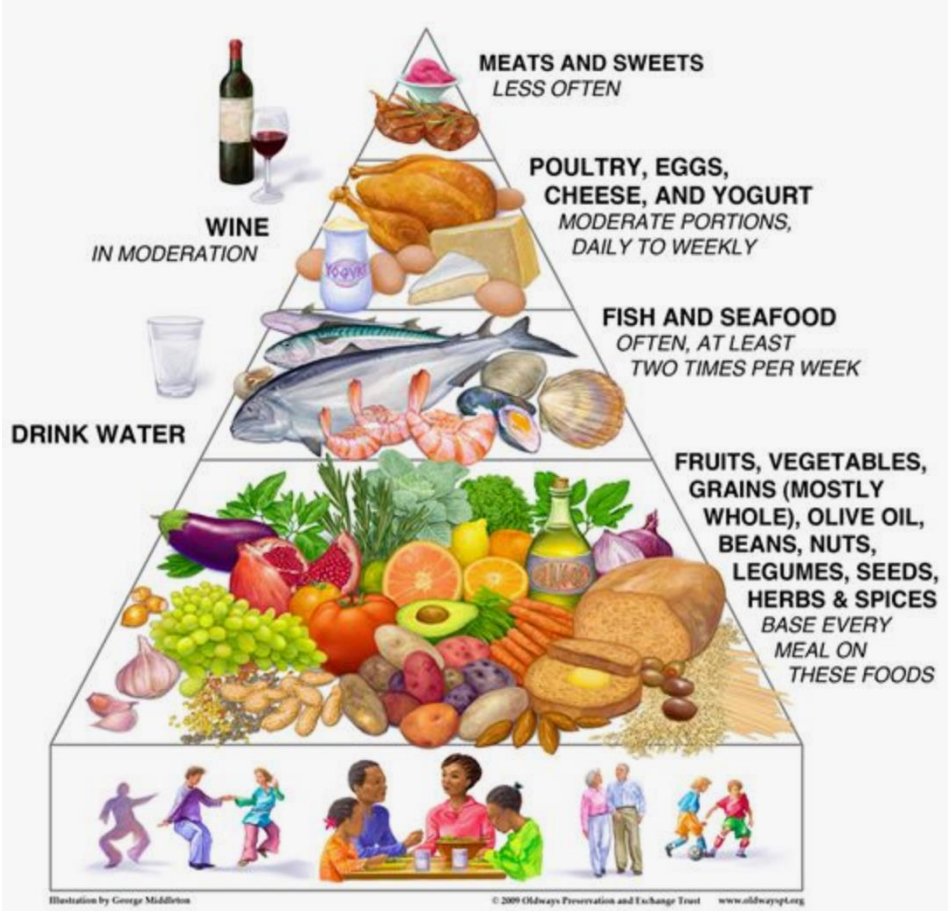
Dietary Fibre, SCFAs & Gut Homeostasis

A varied, plant-based diet > greater microbial diversity = Better health



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Diets and Inflammation
Effective in Non-MPN Disease



- Mediterranean diet adherence associated with reduced all cause mortality
- Individuals with the highest dietary compliance with the Mediterranean diet had (N=3,042):
  - **Inflammatory markers:**
    - 20% lower CRP ($p = 0.015$)
    - 17% lower IL-6 levels ($p = 0.025$).
  - **Coagulation markers**
    - 15% lower homocysteine levels ($p = 0.031$)
    - 14% lower white blood cell counts ($p = 0.001$)
    - 6% lower fibrinogen levels ($p = 0.025$).

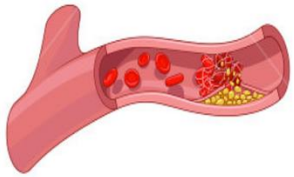
Mitrou et. al. Arch Intern Med. 2007;167(22):2461-2468.
Chrysohoou et. al. *J Am Coll Cardiol.* Jul 7 2004;44(1):152-158. (**Source: R. Scherber, MD**)

Sequelae of Inflammation

Inflammation Contributes to the MPN Phenotype

Inflammation contributes to…











Symptoms

- Fatigue
- Fevers
- Night sweats

Nutritional Deficiencies

- Low cholesterol
- Weight loss

Low blood counts

- Suppressed bone marrow function

Thrombosis

- Reduced production of NO
- Over-stimulated leukocyte activation, cell adhesion molecules
- ET/PV patients with elevated CRP had highest rates of thrombosis

Organ Dysfunction

- Extramedullary hematopoiesis in spleen, liver, lungs
- Portal hypertension following thrombosis

Scherber & Deloughery. "Thrombosis in the MPNs". Hemostatsis and Thrombosisis. Deloughery Editor. 2017. Thromb Haemost. 2010;104(1):151-6; Haematologica. 2009 ;94(11):1484-8. *Leukemia* 2012(26): 563–571; JCO 2015 33(20):2288-2295 (Source: R. Scherber, MD)

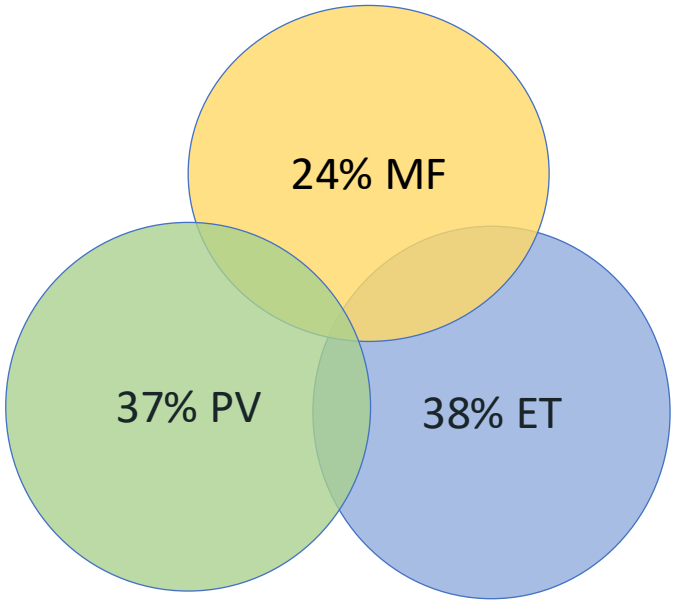
The NUTRIENT Trial

Nutritional Survey: Part IA

(Robyn Scherber MD et al, 2017)

- An internet-based survey hosted by the Mayo Clinic Survey Research Center
- Promoted on multiple MPN-based forums, Facebook pages and websites during February of 2017.
- 55-item questionnaire regarding nutritional and supplement use habits, needs and preferences

N=1329 Respondents
75% Female
Median age 60 years



The NUTRIENT Trial – (Scherber et al, 2017)

Nutritional Survey International Respondents



Poster from ASH 2017, (Scherber, et al)

Nutrition and Supplement Use in The Myeloproliferative Neoplasms: Results from the NUTRIENT Survey

Robyn M. Scherber, MD MPH[1,2], Blake Langlais[3], Holly L. Geyer, MD[4], Amylou Dueck, PhD[3], Carol Johnston, PhD, RD, MS[5], Leslie Padrnos, MD[1], Jeanne Palmer, MD[1], Angela Fleischman, MD PhD[6**], Ruben Mesa, MD FACP[7**]

[1]Hematology and Oncology, Mayo Clinic, Scottsdale, AZ, [2]Hematology and Oncology, Oregon Health and Science University, Portland, OR, [3]Biostatistics, Mayo Clinic, Scottsdale, AZ, [4]Internal Medicine, Mayo Clinic, Scottsdale, AZ, [5]Nutrition, Arizona State University, Phoenix, AZ, [6]Hematology and Oncology, [7]University of California Irvine, Irvine, CA, Cancer Center, UT Health Science Center San Antonio, San Antonio, TX.

**authors contributed equally to this work

BACKGROUND

- **Complementary and alternative medicine** interventions, namely diets and supplements, have demonstrated **anti-inflammatory and anti-oxidant pharmacological properties**.[1-3]
- Myeloproliferative neoplasm (MPN) patients **have increased inflammatory cytokines** (e.g., IL-1, IL-6, IL-8, and TNF-α) that contribute to **symptom burden** (e.g., fatigue, pruritus, night sweats, bone pain) and **nutritional deficiencies** (e,g., hypocholesterolemia, hypoalbuminemia, weight loss).
- To date no studies have evaluated the **habits, needs, and preferences of nutritional and supplement use interventions** among an MPN population.

OBJECTIVES

The aim of this project was to better understand the nutritional and supplement use characteristics in an MPN population that will help inform the creation of tailored dietary and supplement interventions.

MATERIALS & METHODS

- An internet-based survey was hosted by the Mayo Clinic Survey Research Center and promoted on multiple MPN-based forums, Facebook pages and websites during February of 2017.
- The survey included data on demographics, MPN characteristics, nutritional habits, supplement use, and symptom burden using the MPN Symptom Assessment Form Total Symptom Score (MPN-SAF TSS)/MPN-10.[3]
- T tests and chi square tests compared group means and frequencies, respectively.

PARTICIPANTS

Demographics and symptom burden: **1329 international MPN patients** responded to the online survey of which 1131 respondents completed ≥10 multiple choice questions, and were age 18 years or older.

- **Country of origin** of respondents is demonstrated in Figure 1. The highest proportion of respondents were from the United States (50.2%), United Kingdom (31.9%), Australia (5.2%), and Canada (3.5%).
- Average MPN-SAF TSS score was 33.6/100 (SD=17).

RESULTS



Figure 1. Countries representing respondents to the MPN nutritional and supplement use survey (N=1131).

Nutrition: Overall, 34% of respondents endorsed using diet to help control their symptoms or MPN disease.

- **23%** of respondents endorsed having **food allergies or intolerances** (Table 1).
- **31%** of individuals followed a **specific diet** or had **dietary restrictions**.

Food Allergies and/or Intolerances	Frequency among respondents
Milk	8.3%
Wheat	6.9%
Fruit	4.1%
Shellfis	2.8%
Soy	2.3%
Peanuts	1.7%
Egg	1.4%
Tree Nuts	1.4%
Fish	1.3%
Dietary Restrictions	
Low Salt	6.6%
Gluten-free	6.5%
Mediterranean diet	6.0%
Vegetarian	5.7%
Low Fat	5.3%
Anti-inflammatory	5.1%
Lactose Intolerant	3.9%
Supplement Use	
Vitamin D	28.7%
Multivitamin/mineral	22.7%
Calcium	16.5%
Vitamin B12	13.8%
Curcumin	8.8%
CoQ10	7.6%
Digestive enzymes	7.2%
Antioxidants	6.4%

Table 1. Frequency of dietary allergies, intolerances, restrictions and supplement use among a cohort of MPN patients (N=1131).

Supplement Use: **72%** of MPN respondents reported use of **over the counter supplements**.

- MPN-10 symptom scores were compared for specific supplements between users and non-users (Table 2).
- Supplement use was significantly more common among **females (74%)** than among males (66%, *P*=0.01).

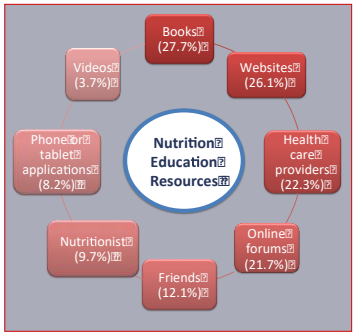


Figure 2. Nutrition Education Resources among MPN Patients

***Nutritional Education Preferences*: 34.0%** of patients endorsed **using diet** to help control their **symptoms** or **MPN disease**.

- Patients utilized a variety of resources for nutritional education (Figure 2).
- **96.2%** of patients endorsed being **willing to restrict their diet** if it helped to control symptom burden.
- **98%** of patients were **willing** to restrict their diet if it could stabilize their MPN.

Correlative	Mean Symptom Burden (MPN-10)		Correlation	P-value
Diet	**Not Following Diet**	**Following Diet**	**T-value**	**P-value**
Diabetic diet	3.33	4.67	-4.58	<0.0001
Lactose Intolerant	3.35	3.87	-2.08	0.433
Food Intake (Dichotomous)	**Never**	**At Least Once Per Week**	**T-value**	**P-value**
Alcohol	3.62	3.11	4.92	<0.0001
Fast Food	3.24	3.59	-3.19	0.0015
Fried Foods	3.22	3.46	-2.33	0.0198
Rice	3.57	3.30	2.01	0.0452
Soda	3.22	3.72	-4.08	<0.0001
Food Intake (Continuous)			**Pearson**	**P-value**
Alcohol	-	-	-0.139	<0.0001
Baked Goods	-	-	-0.070	0.0212
Dairy other than Cheese	-	-	-0.069	0.0240
Fast Food	-	-	0.104	0.0007
Fried Foods	-	-	0.086	0.0051
Pasta	-	-	-0.072	0.0183
Pre-made Snack Foods	-	-	0.067	00296
Soda	-	-	0.121	<0.0001
Refined Sugars	-	-	0.075	0.0139
Tacos	-	-	0.068	0.0277

Table 2. Associations between dietary habits and restrictions with MPN-10 symptom score among MPN patients.

Supplement	Percentage Using	Mean Symptom Burden (MPN-10)		
		Taking Supplement	**Not Taking Supplement**	**P-value**
Amino Acids	3.7%	2.8	3.4	0.02
N-Acetylcysteine	0.9%	2.4	3.4	0.02
Bach Flowers	0.9%	5.2	3.4	0.008

Table 3. Associations between supplement use and MPN-10 symptom score among MPN patients.

SYMPTOM BURDEN ASSOCIATIONS

- Intake of **alcohol** (*P*<0.0001), **baked foods** (*P*=0.02), **dairy other than cream** (*P*=0.02), and **pasta** (*P*=0.02) was associated with **significantly lower TSS** when analyzed as a continuous variable based on frequency of intake over an average week (Table 2).
- Fast food (*P*=0.0007), pre-made snacks (*P*=0.03), soda (*P*<0.0001), refined sugar (*P*=0.01), and taco (*P*=0.03) intake was associated with **worsened symptom score**.
- **Symptom burden was significantly lower** among individuals using **amino acid supplements** (*P*=0.02) and **N-Acetylcysteine** (*P*=0.02) and significantly higher in individuals taking **Bach flowers** (*P*=0.008, Table 3).

CONCLUSIONS

- Currently **no consensus recommendations** exist for the **nutritional management of MPN patients.**
- MPN patients often **seek out and employ dietary restrictions**, at times as a method to help manage their MPN disease.
- **Weak but significant** correlations exist between **diet** and **MPN-related symptom burden**.
  - Prospective trials are needed to determine clinical relevance of these associations.
- **Nutrition represents a possible low risk adjunct therapy** which could be combined with traditional treatments to help manage the MPN disease course.
  - These results will be used to inform the creation of an MPN nutritional intervention with the goal of improving symptom burden and reducing inflammation

REFERENCES

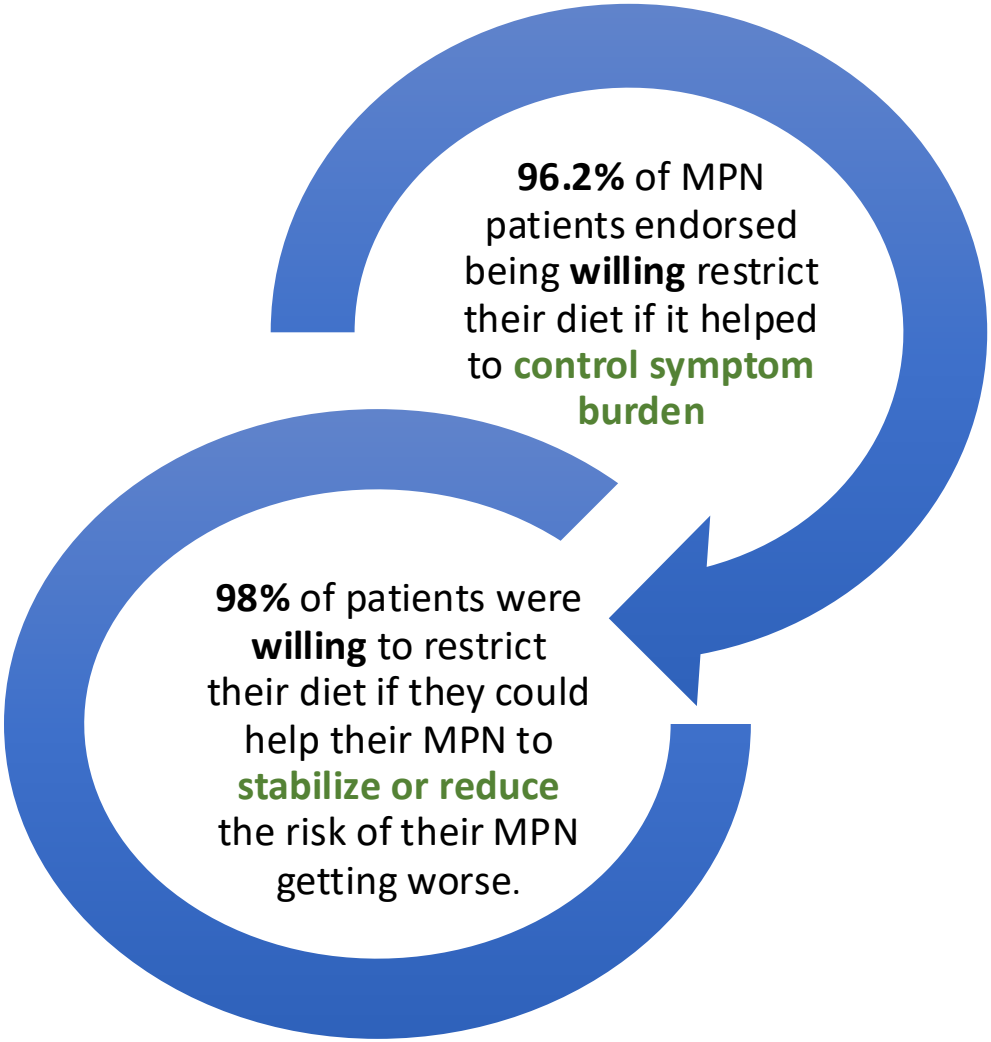
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4. Emanuel RM, Dueck AC, Geyer HL, et al. Myeloproliferative neoplasm (MPN) symptom assessment form total symptom score: prospective international assessment of an abbreviated symptom burden scoring system among patients with MPNs. *J Clin Oncol* 2012;30(33):4098-103.

MORE INFORMATION

Scherber@ohsu.edu

@RobynScherber

The NUTRIENT Trial- Patient preference: (Scherber et al, 2017)



MPN NUTRIENT study
Robyn Scherber MD, et al. 2017: Part A1

- 1st study investigating impact of diet on MPN symptoms & inflammatory cytokines. (N=1329)

Conclusions:

1. MPN pts. seek dietary methods to manage MPN symptoms.
2. **<u>Weak but significant correlation</u>** between diet & worsened MPN symptoms. (fast food, refined sugar, premade snacks, soft drinks)
3. **Next** – Develop evidence-based dietary interventions to reduce MPN symptoms & inflammatory biomarkers, improve QoL & hopefully delay progression.







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The NUTRIENT Trial – (Scherber et al, 2017-18)

Part II: Feasibility and Adherence to a Diet Intervention

Enrollment N=30

Meeting with a nutritionist for diet education

- **Blood draw**
- **BMI**

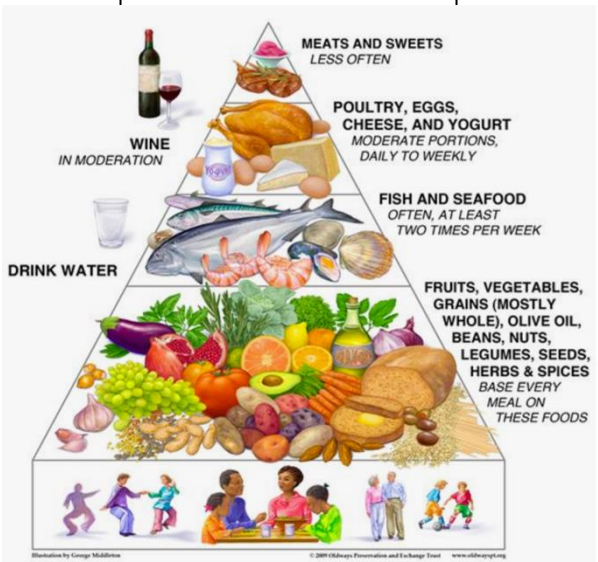
Baseline — 6 weeks — 12 weeks

- **24-Hour Diet recall**
- **MPN-10**

Primary Endpoint: combined >70% Dietary Adherence and >5/10 patient-reported feasibility

Secondary endpoint:
BMI
percentage body fat
nutritional markers
inflammatory markers
plasma cytokines
JAK2 allele burden

MPN RESEARCH FOUNDATION
advancing blood cancer research



MPN Microbiome Project

Ass. Prof Angela Fleischman, MD University of California

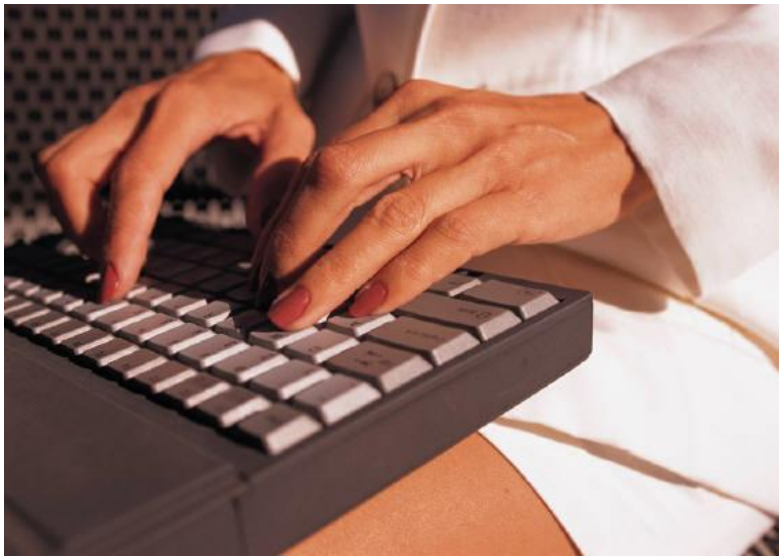
- Recruiting 60 pairs of MPN pts. & their spouses to supply stool samples.

- DNA sequencing will investigate whether MPN pts. have different gut microbiomes.
  - To participate: agf@uci.edu

- Microbiome testing not yet used diagnostically. Research only.

- Caution - private labs offer bacterial stool analysis. (not DNA sequencing)
  - But – $$$
  - Limited usefulness. Most gut bugs are anaerobic so can't be cultured!
  - DNA sequencing is more accurate, but not used clinically yet!

- Watch this space….???



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Getting enough fibre?
A healthy gut is like a healthy river ecosystem!







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Bristol Stool Chart

X	Type 1	Separate hard lumps, like nuts (hard to pass)
X	Type 2	Sausage-shaped but lumpy
✓	Type 3	Like a sausage but with cracks on its surface
✓	Type 4	Like a sausage or snake, smooth and soft
	Type 5	Soft blobs with clear-cut edges (passed easily)
X	Type 6	Fluffy pieces with ragged edges, a mushy stool
X	Type 7	Watery, no solid pieces. **Entirely Liquid**

Healthy Eating Tips for MPN

- Eat a varied, high-fibre, **mostly plant food** diet.

  = **Increased gut microbial diversity = BETTER HEALTH**

  - Veg, fruit, whole grains, legumes, nuts & seeds.
  - oats, rye bread, firm bananas, cooked & cooled rice, pasta, potatoes, unsalted nuts. (resistant starch)
- Eat 3 different veg with main meal = **½ plate area.**
- Include fermented foods - Natural yoghurt, sauerkraut, kimchi etc.
- Increase fibre slowly to improve tolerance. Drink plenty of water.
- Fill shopping trolley with **five food group** foods.
- Think **EVERYDAY** & **SOMETIMES** foods!
- Small, gradual dietary changes = positive impacts long-term!
- *Look after your gut bugs & they'll look after you!*







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My kitchen-laboratory!
Sauerkraut, kimchi & kombucha ferments.











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Websites: Healthy eating & the microbiome

CSIRO Healthy Diet Score:
https://my.totalwellbeingdiet.com/healthy-diet-score

Take the Healthy Eating Quiz: https://daa.asn.au/smart-eating-for-you/smart-eating-fast-facts/healthy-eating/

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How the food you eat effects your gut. Dr Shilpa Revella 2017
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Acknowledgements:
NUTRIENT Trial slides and information:

Robyn M. Scherber, M.D., M.P.H.
Fellow, Department of Hematology and Oncology
Oregon Health and Science University, 3181 SW Sam Jackson Park Rd
Portland, OR 97239 Cell phone: 612-481-7912

After July 1st 2018:
Assistant Professor of Medicine, Department of Hematology & Oncology
Mays Cancer Center at UT Health San Antonio MD Anderson
Mail Code 8026, 6th Floor Urschel Tower 7979 Wurzbach Rd
San Antonio, TX 78229-3900 Email: Scherber@uthscsa.edu

Angela G. Fleischman M.D. Ph.D. | Assistant Professor
Department of Medicine, Division of Hematology/Oncology
UC Irvine Health, 839 Medical Sciences Court
Sprague Hall B100 Irvine, CA 92697
Tel: 949-824-2559 (office), 949-824-4144 (lab)
Fax: 888-857-1020, Email: agf@uci.edu, Website: www.mpnlab.org

Ruben A. Mesa, MD, FACP
Director Mays Cancer Center at UT Health San Antonio MD Anderson
Mays Family Foundation Distinguished University Presidential Chair
Professor of Medicine, Office Phone: 210-450-1406, Fax: 210-450-1100, Cell: 507-250-2508
mesar@uthscsa.edu

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Questions???
















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