

What MPN Patients Have Taught US

Ruben A. Mesa, MD, FACP

Professor and Chair, Division of Hematology & Medical Oncology

Deputy Director, Mayo Clinic Cancer Center

Arizona, USA

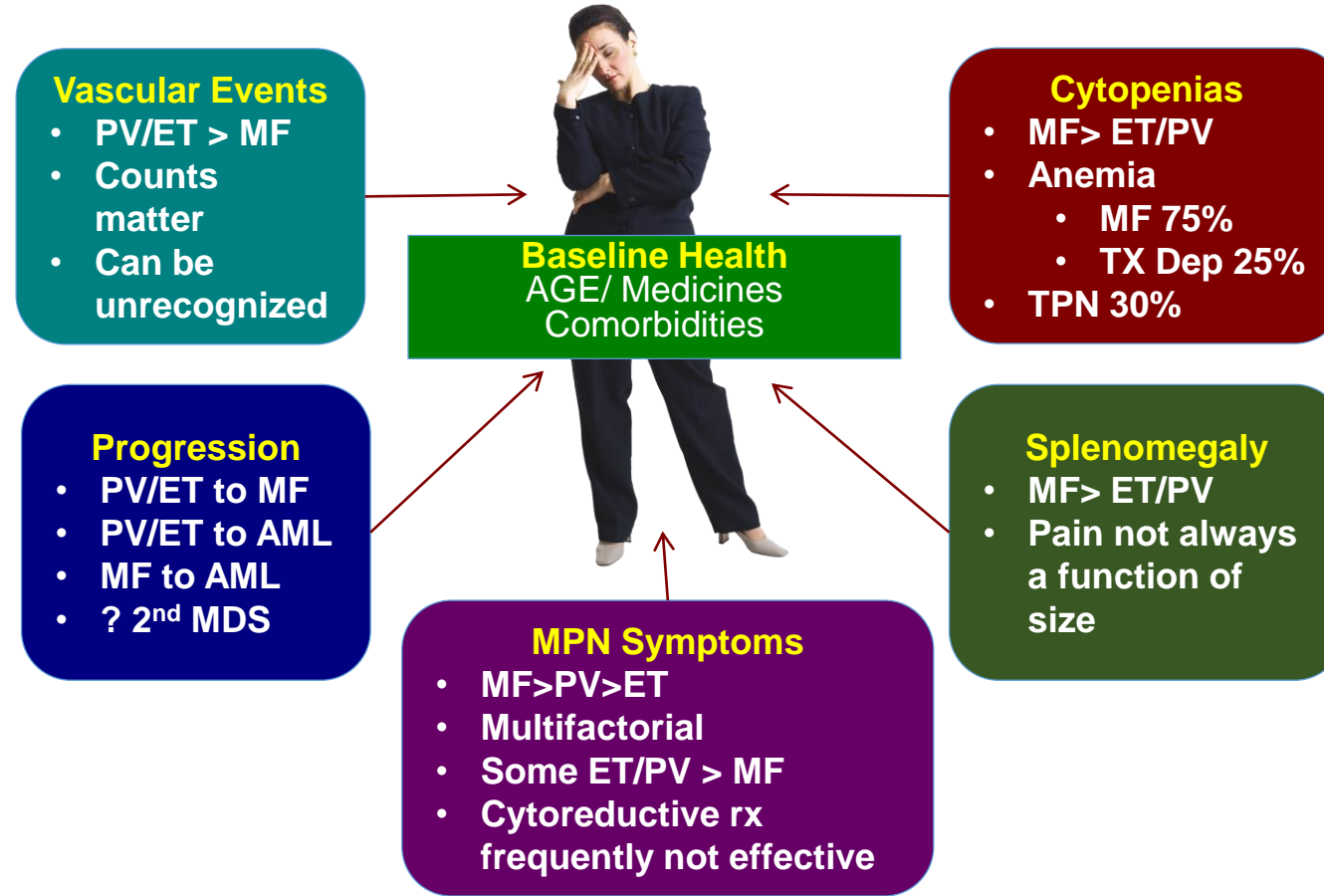
mesa.ruben@mayo.edu

What Have MPN Patient Taught US?

1. Burden of having an MPN includes several clinical features including MPN associated symptoms
2. Symptoms are heterogeneous and variable across MPN subtype and risk
3. MPN symptoms correlate with disease biology, risk, possibly progression?
4. Burden of having an MPN extends beyond symptoms to distress and employment
5. Tracking symptom changes relevant for measuring value of medical treatments
6. Non pharmacologic options may have a role, alongside medicines or transplant, in MPN patient health and QoL

Assessing MPN Burden

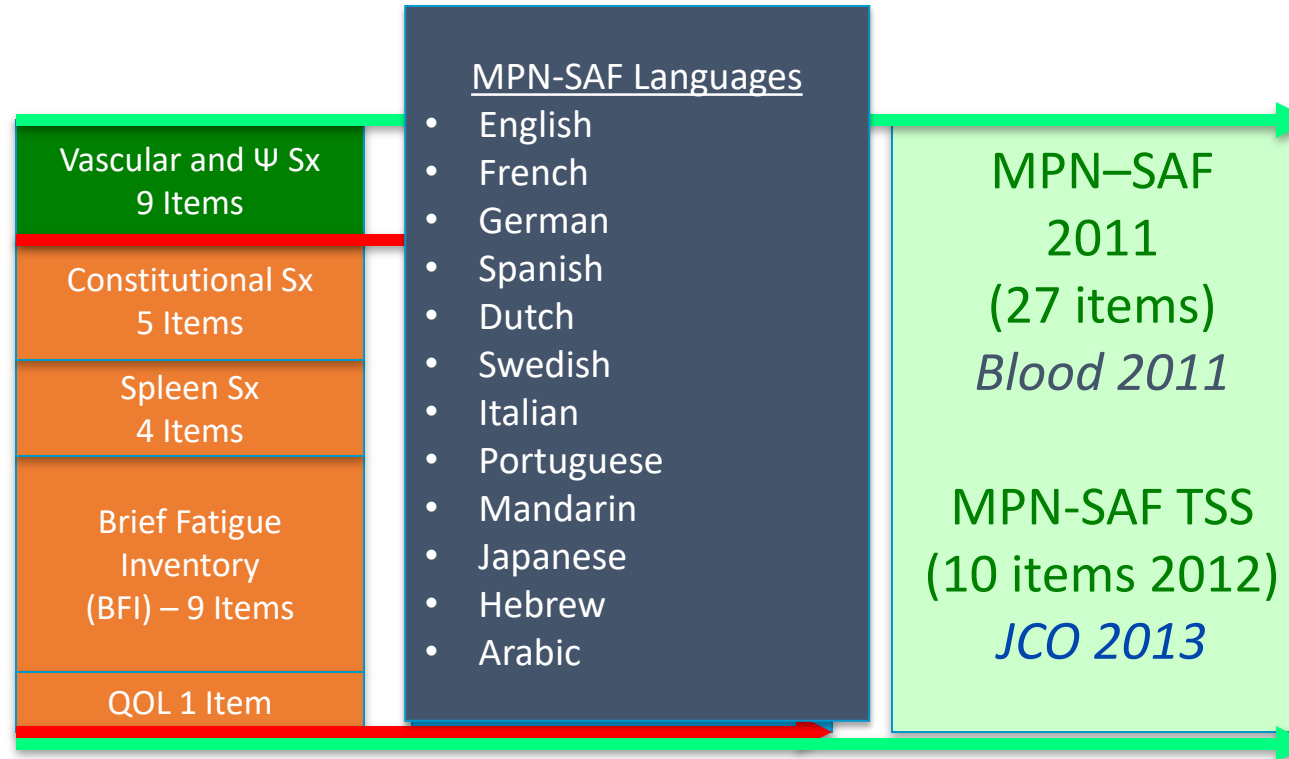
WHO Diagnosis Does Not Tell Whole Story



MPN SYMPTOMS



Evolution of MPN Symptom Assessment Tools



MPN SAF TSS “MPN10” in Many Languages

English



Name: _____

Date: _____

Fill out the form below to track the burden of your symptoms.

Symptom: 1 to 10, 0 if absent and 10 being worst imaginable

Please rate your fatigue (weariness, tiredness) by circling the one number that best describes your WORST level of fatigue during the past 24 hours

Fatigue	0	1	2	3	4	5	6	7	8	9	10
(ABSENT)											(WORST IMAGINABLE)

Circle the one number that describes how much difficulty you have had with each of the following symptoms during the past week

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Problems with concentration - compared to before my diagnosis	0	1	2	3	4	5	6	7	8	9	10
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Night sweats	0	1	2	3	4	5	6	7	8	9	10
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Bone pain (diffuse, not joint pain or arthritis)	0	1	2	3	4	5	6	7	8	9	10
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Fever (> 37.8°C or 100°F)	0	1	2	3	4	5	6	7	8	9	10
(ABSENT)											(DAILY)

Unintentional weight loss last 6 months	0	1	2	3	4	5	6	7	8	9	10
(ABSENT)											(WORST IMAGINABLE)

To help you get a clear overall picture of how you are feeling, you can add up all your scores to calculate your Total Symptom Score.

Total:

You can also fill in this form and find more expert information about myeloproliferative neoplasms online at www.spotlightonMPN.com

Arabic

نموذج تقييم الأعراض

الاسم: _____

التاريخ: _____

إملأ نموذج التقييم التالي لتتبع الأعراض التي تتعرض إليها.

الأعراض: تتدرج من ١ إلى ١٠. صفر في حالة غياب العرض و ١٠ هي أسوأ ما يمكنك تخيل حدونه.

يرجى تحديد مستوى الإرهاق (الضعف، الإجهاد) عن طريق وضع دائرة حول الرقم الذي تراه يصف أقصى حالات الإرهاق التي تعرضت إليها خلال الـ ٢٤ ساعة الماضية.

الإرهاق	١٠	٩	٨	٧	٦	٥	٤	٣	٢	١	صفر
(غياب العرض)											

ضع دائرة حول الرقم الذي يمثل مدى الضغوطات التي واجهتها مع كل من الأعراض التالية خلال الأسبوع الماضي

الإحساس بالشبع السريع عند الأكل (الشبع المبكر)	١٠	٩	٨	٧	٦	٥	٤	٣	٢	١	صفر
(غياب العرض)											

عدم ارتياح في البطن	١٠	٩	٨	٧	٦	٥	٤	٣	٢	١	صفر
(غياب العرض)											

الحمول	١٠	٩	٨	٧	٦	٥	٤	٣	٢	١	صفر
(غياب العرض)											

مشاكل في التركيز - مقارنةً بقيل تشخيصي	١٠	٩	٨	٧	٦	٥	٤	٣	٢	١	صفر
(غياب العرض)											

التعرق الليلي	١٠	٩	٨	٧	٦	٥	٤	٣	٢	١	صفر
(غياب العرض)											

الحكة	١٠	٩	٨	٧	٦	٥	٤	٣	٢	١	صفر
(غياب العرض)											

آلام العظام (منتشرة، ليس آلام المفاصل أو التهاب المفاصل)	١٠	٩	٨	٧	٦	٥	٤	٣	٢	١	صفر
(غياب العرض)											

ارتفاع درجة حرارة الجسم (> ٣٧,٨°C أو > ١٠٠.٢°F)	١٠	٩	٨	٧	٦	٥	٤	٣	٢	١	صفر
(غياب العرض)											(يوميًا)

فقدان الوزن الغير مقصود خلال الـ ٦ أشهر الماضية	١٠	٩	٨	٧	٦	٥	٤	٣	٢	١	صفر
(غياب العرض)											

كي تتمكن من مساعدتك على الحصول على صورة شاملة عن ما تشعرين به، يمكنك جمع درجات التقييم لمعرفة

مجموع نقاط الأعراض.

يمكنك ملئ هذا النموذج و الحصول على معلومات أكثر عن أورام النكاثر النقي عن طريق زيارة

www.spotlightonMPN.com

Adapted from Emanuel et al. J Clin Oncol. In press

MPN10: allows visual assessment

MPN 10 KNOW YOUR SCORE

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NOVARTIS ONCOLOGY Neovartis Pharma AG CH-4002 Basel Switzerland © Novartis 2014 May 2014 G-INC-1090831

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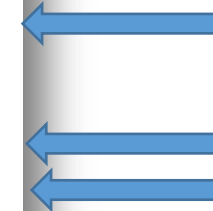
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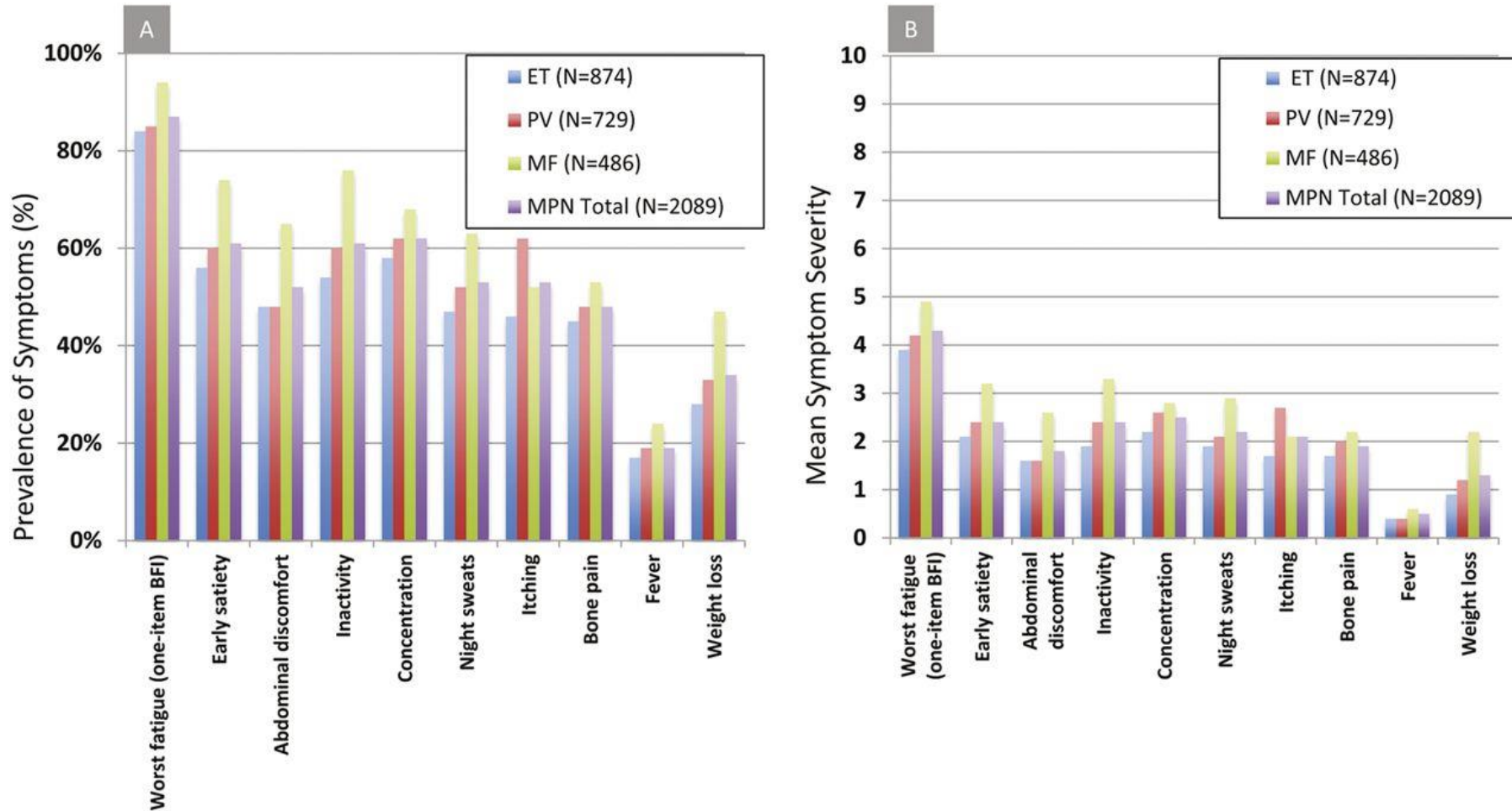
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1. Emanuel RM, et al. *J Clin Oncol*. 2012;30:4098-4103.

Classic Signs and Symptoms of MPNs



What is MPN Symptom Burden in Patients vs. General Population?

MOSAICC Population Vs. Controls

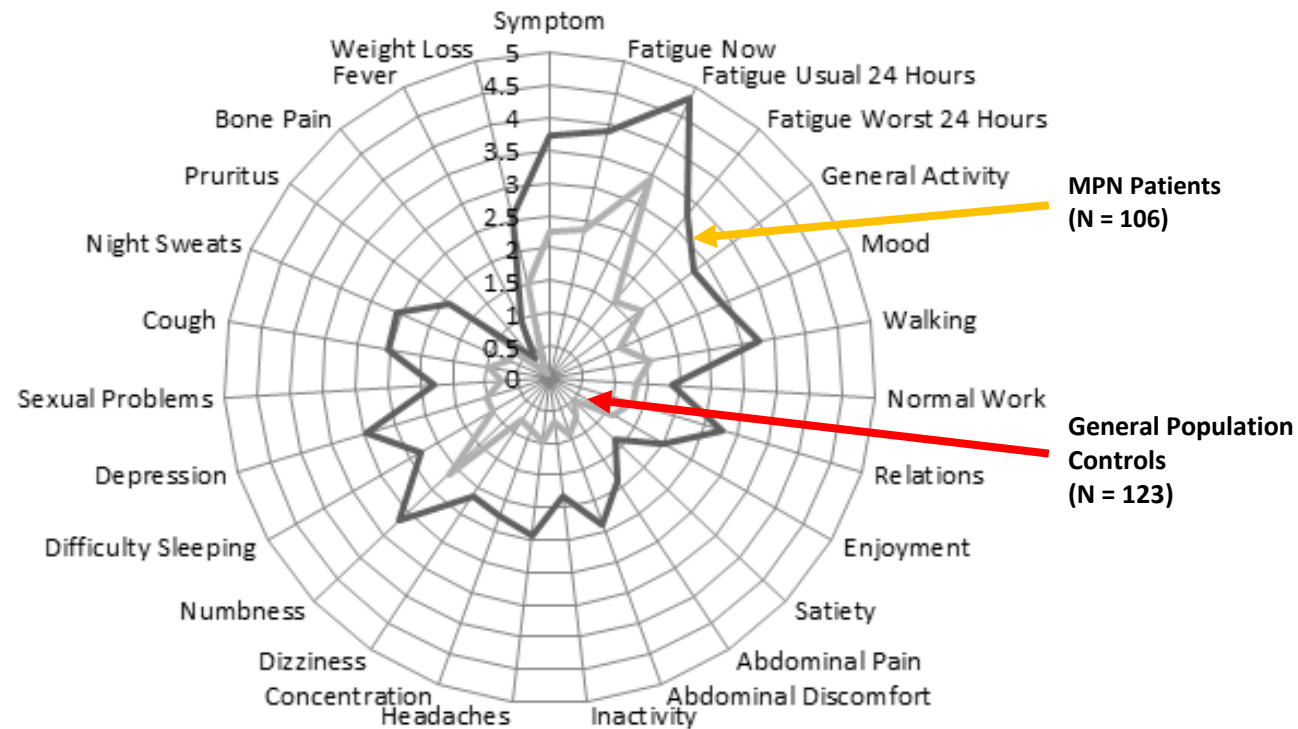


Image courtesy of Ruben A. Mesa, MD

Definitions

HRQOL in MPNs?

Σ

- MPN related symptoms
- Medication related toxicities
- Problems from prior MPN complications
- Stressors from having their MPN
 - Financial
 - Emotional
 - Intrapersonal
- Co-morbidities
- Hassle of medical care

What Have MPN Patient Taught US?

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What is “Symptomatic” in MF, enough to consider Rx?

Analysis of 425 MF with MPN-10, DIPSS Risk, Spleen Size

Table 1: Ordinal logistic regression models of DIPSS risk score (N=420) by symptoms in JAK2-naïve myelofibrosis patients.

Model	DIPSS Risk AIC
TSS >20	936.657*
Worst single symptom score >5	935.281*
Worst single symptom score >6	942.198
Worst single symptom score >7	942.684
TSS >20 & single score >5	938.510
TSS >20 & single score >6	943.335
TSS >20 & single score >7	944.867

*Optimal models based on lowest AIC.

Single Item
>5 (out of 10)

TSS
>20 (out of 100)

Scherber et. al. ASH 2016

What is “Symptomatic” in ET or PV in HU Failure,
enough to consider Rx?

Analysis of 838 PV/ 867 ET with Disease Features

Single Item

>5 (out of 10)

TSS

>20 (out of 100)

Meeting Threshold

- Prior Vascular Events
- Lower Hb (even without anemia)
- Higher WBC
- ? Different molecular features

Scherber et. al. ASH 2016

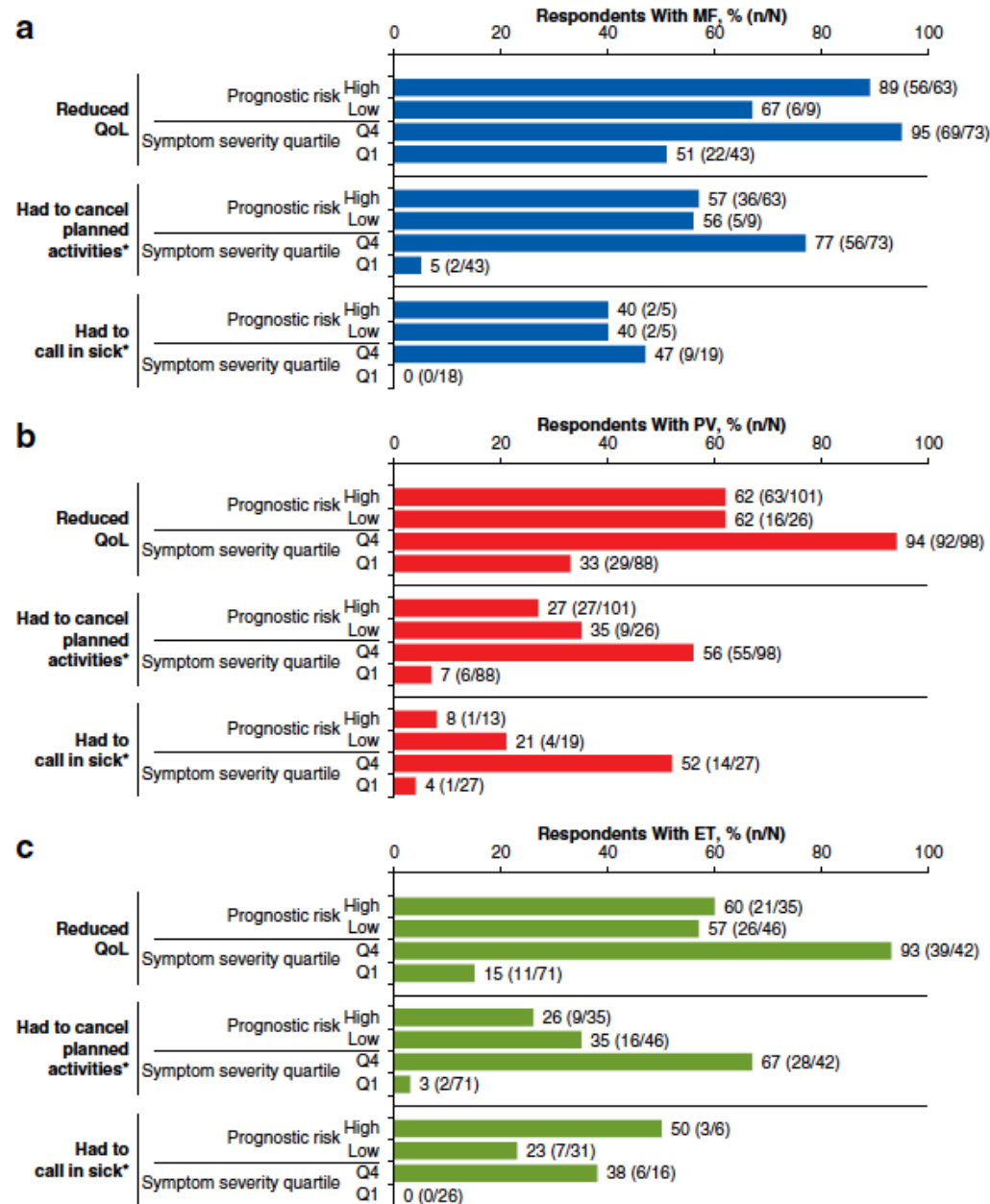


Fig. 1 Impact of MPNs on QoL, work, and activities of daily living. MPN impact was stratified by calculated prognostic risk score and symptom severity quartile in respondents with (a) MF, (b) PV, and (c) ET. ET = essential thrombocythemia; MF = myelofibrosis; MPN = myeloproliferative neoplasm; PV = polycythemia vera; Q1 = quartile 1; Q4 = quartile 4; QoL = quality of life. * ≥ 1 day in the preceding 30 days

Mesa et. al.
BMC Cancer
2016;16:167

Investigating MPN Heterogeneity-Geyer 2014

Regular Article

Blood 2014

MYELOID NEOPLASIA

Distinct clustering of symptomatic burden among myeloproliferative neoplasm patients: retrospective assessment in 1470 patients

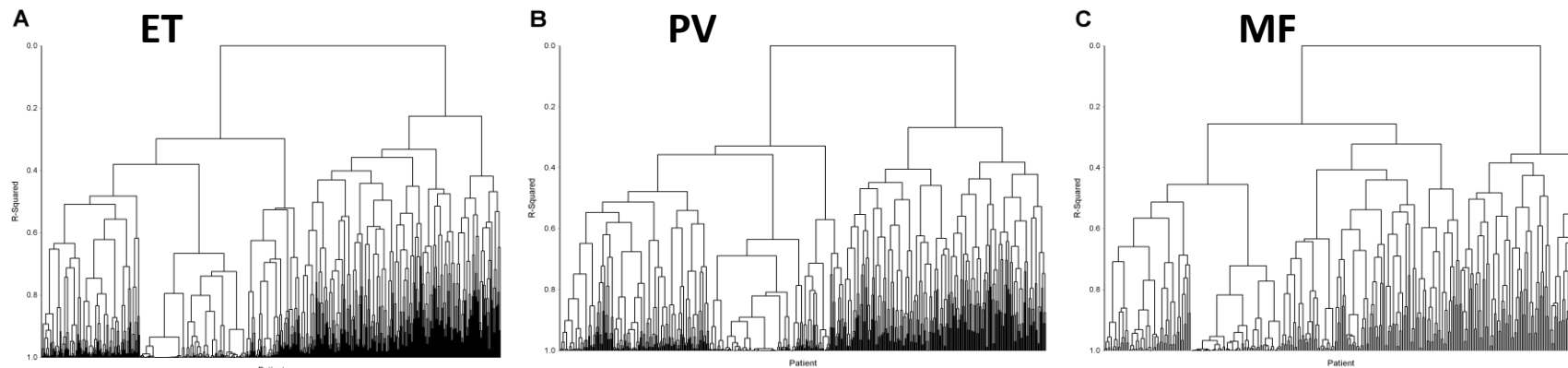
Holly L. Geyer,¹ Robyn M. Emanuel,¹ Amylou C. Dueck,² Jean-Jacques Kiladjian,³ Zhijian Xiao,^{4,5} Stefanie Slot,⁶ Sonja Zweegman,⁶ Federico Sackmann,⁷ Ana Kerguelen Fuentes,⁸ Dolores Hernández-Maraver,⁸ Konstanze Döhner,⁹ Claire N. Harrison,¹⁰ Deepti Radia,¹⁰ Pablo Muxi,¹¹ Carlos Besses,¹² Francisco Cervantes,¹³ Peter L. Johansson,¹⁴ Bjorn Andreasson,¹⁴ Alessandro Rambaldi,¹⁵ Tiziano Barbui,¹⁵ Alessandro M. Vannucchi,¹⁶ Francesco Passamonti,¹⁷ Jan Samuelsson,¹⁸ Gunnar Birgegård,¹⁹ and Ruben A. Mesa²⁰

¹Division of Hospital Internal Medicine and ²Section of Biostatistics, Mayo Clinic, Scottsdale, AZ; ³Clinical Investigation Center, Hospital Saint-Louis, Paris, France; ⁴MDS and MPN Centre, Institute of Hematology and Blood Diseases Hospital and ⁵State Key Laboratory of Experimental Hematology, Institute of Hematology and Blood Diseases Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Tianjin, China; ⁶Department of Hematology, VU University Medical Center, Amsterdam, the Netherlands; ⁷Fundaleu, Buenos Aires, Argentina; ⁸Department of Haematology, University Hospital La Paz, Madrid, Spain; ⁹Department of Internal Medicine III, University Hospital of Ulm, Germany; ¹⁰Department of Haematology, Guy's and St. Thomas NHS Foundation Trust, London, UK; ¹¹Unidadde Hematologia, Hospital Británico, Montevideo, Uruguay; ¹²Hematology Department, Hospital del Mar, Barcelona, Spain; ¹³Hematology Department, Hospital Clinic, IDIBAPS, University of Barcelona, Spain; ¹⁴Internal Medicine, NU Hospital Organization, Uddevalla, Sweden; ¹⁵Unit of Hematology, Azienda Ospedaliera Papa Giovanni XXIII, Bergamo, Italy; ¹⁶Hematology Division of Hematology, Ospedale di Circolo, Varese, Italy; ¹⁷Department of Hematology, Fondazione IRCCS Policlinico San Matteo, University of Pavia, Pavia, Italy; ¹⁸Department of Internal Medicine, Stockholm South Hospital, Stockholm, Sweden; ¹⁹Department of Hematology, University Hospital, Uppsala, Sweden; and ²⁰Department of Hematology/Oncology, Mayo Clinic, Scottsdale, AZ

•Prospective Study

•1470 MPN Patients

•DIPSS/IPSET/Leukemia 2013 PV Criteria



Investigating MPN Heterogeneity-Geyer 2014

5 ET Clusters

MPN-SAF TSS

Gender

Language

Lab abnormalities

Hx of hemorrhage

5 PV Clusters

MPN-SAF TSS

Age

Gender

Language

Lab abnormalities

Hx of hemorrhage

4 MF Clusters

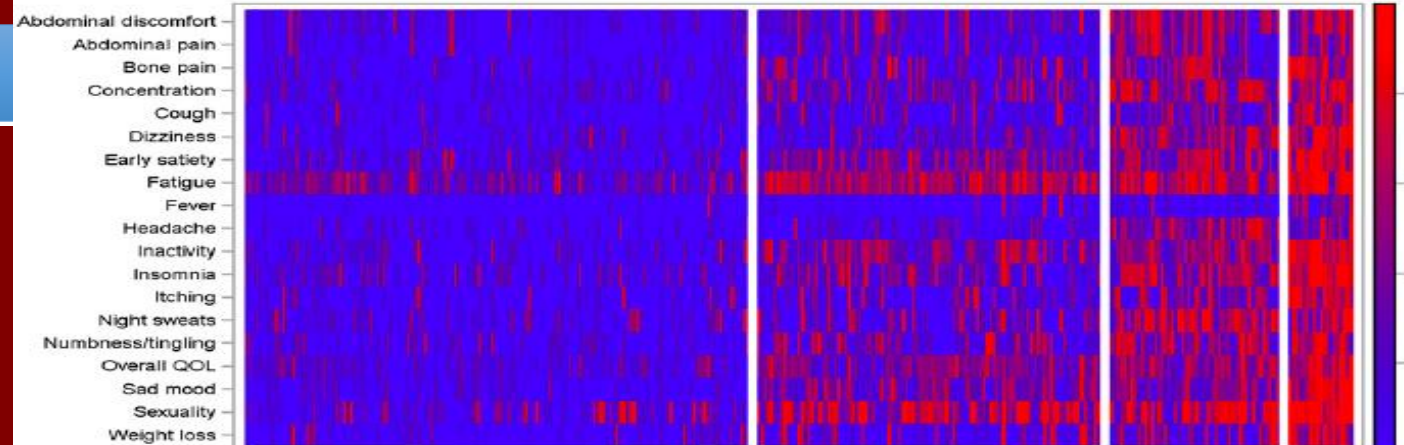
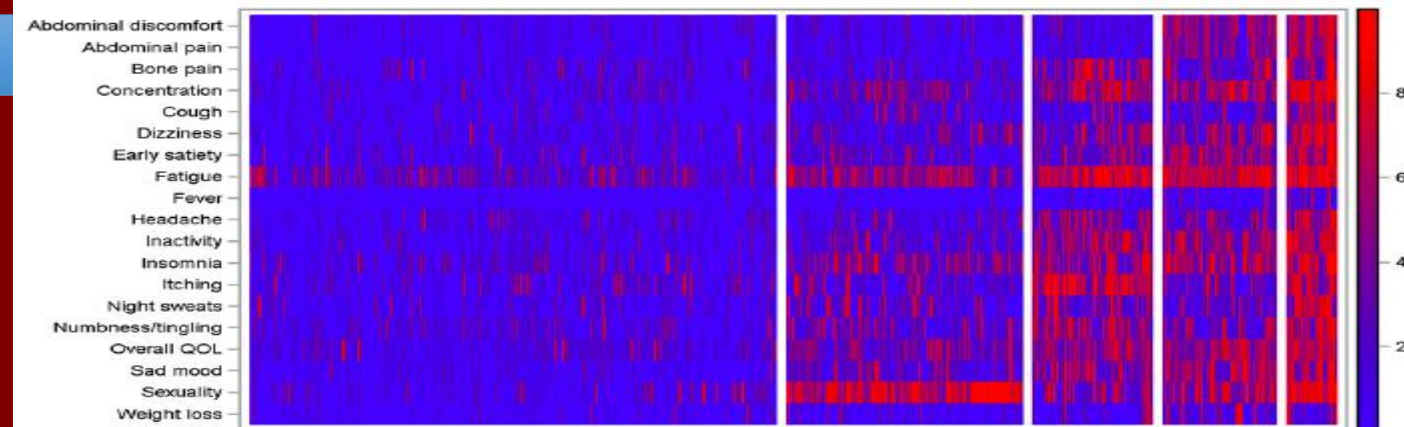
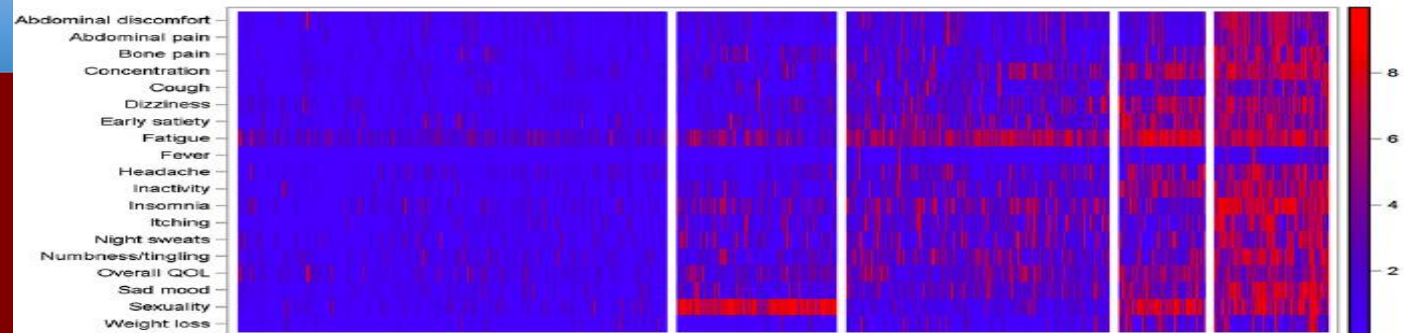
MPN-SAF TSS

DIPSS Risk

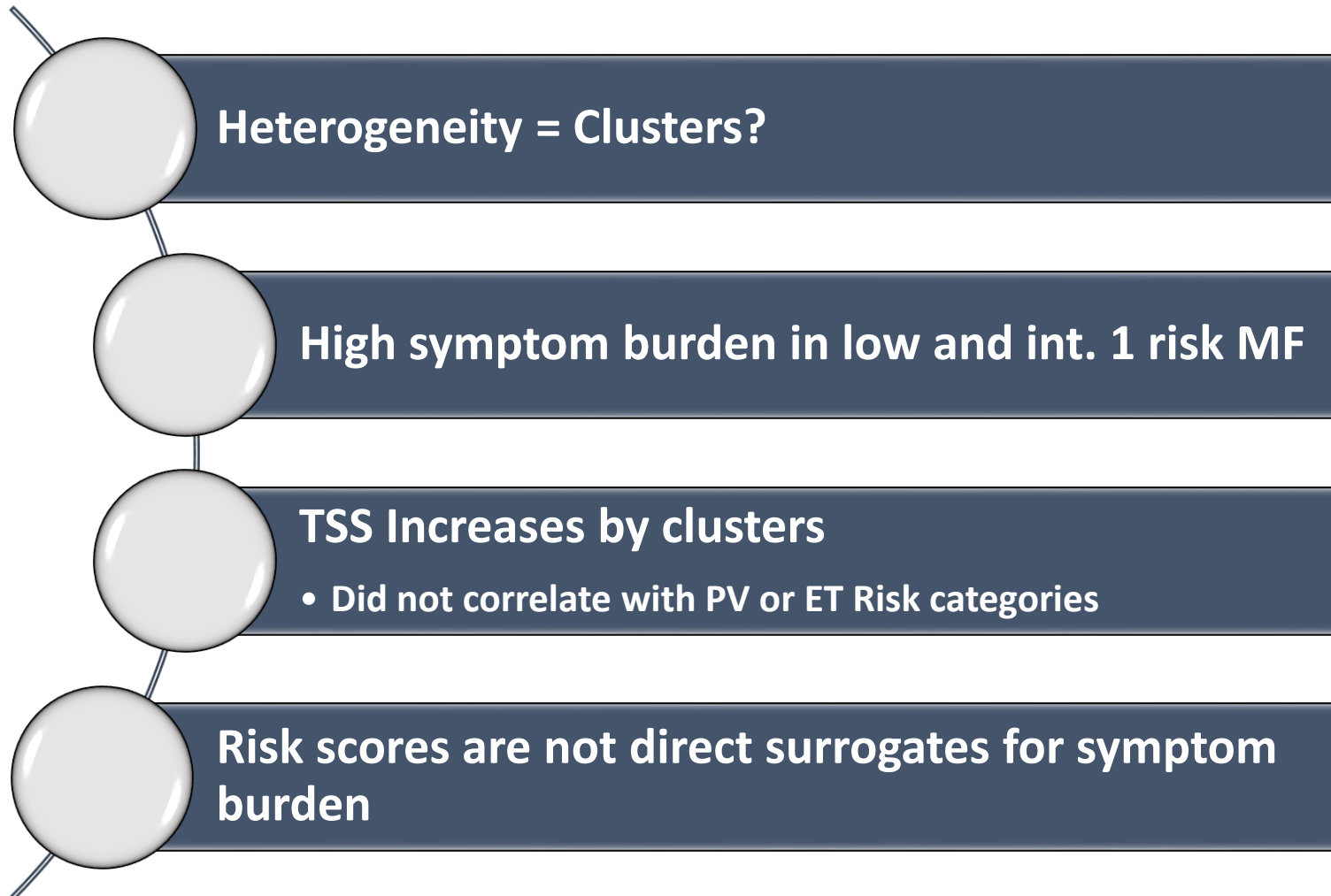
Leukopenia

Thrombocytopenia

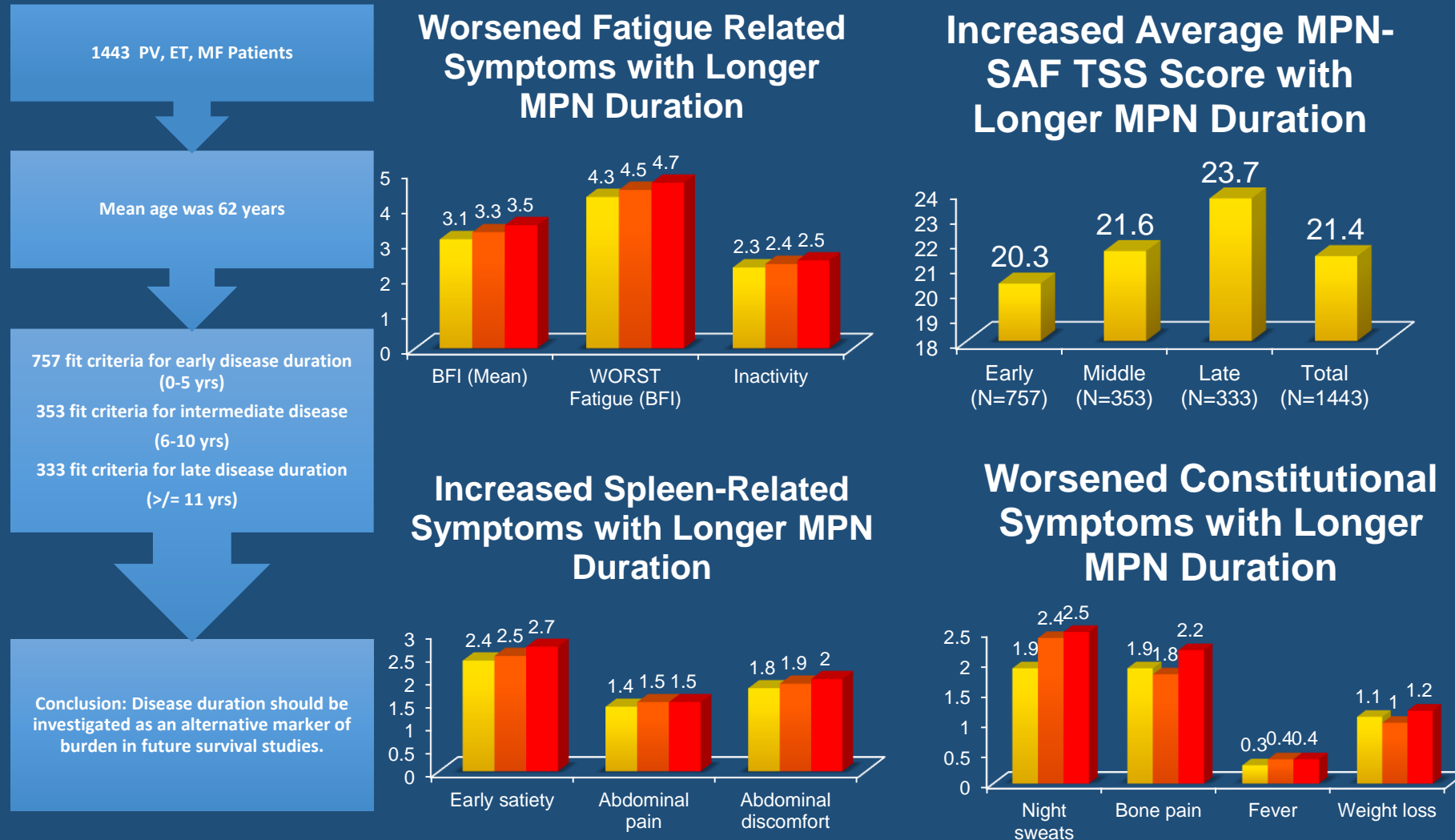
Spleen size



Investigating MPN Heterogeneity-Geyer 2014



Impact of Disease Duration on Symptoms



Once Size Does Not Fit All: *The MPN Gender Study*

Females

- Lower rate of thrombocytopenia (8% vs 14%, $p < 0.001$).
- Higher TSS (adjusted mean 23.9 vs 20.6, $p < 0.001$)
- Higher symptom scores for 15/18 items
- Prominent symptoms: *fatigue, bone pain, abdominal discomfort, and microvascular related*

Males

- Higher mean age than females (mean 60.7 yrs [SD 12.6] vs 59.3 yrs [SD 14.4]; $p = 0.02$)
- Higher rate of requirement for red blood cell transfusion (7% vs 5%, $p = 0.02$)
- Higher mean white blood cell count (mean $9.5 \times 10^9/L$ [SD $8.2 \times 10^9/L$] vs mean $8.5 \times 10^9/L$ [SD $6.1 \times 10^9/L$]; $p = 0.004$)

Females demonstrate...

Higher levels of fatigue

- Younger
- Lower red blood counts
- Lower transfusion rates

More Abdominal Symptoms

- Male=female abdominal thrombosis rates

Microvascular symptoms

- Previous reports show more macrovascular symptoms

Higher Total Symptom Scores

- Male=female QOL score

MPN *Insomnia*

- Included 1992 MPN Patients
- BFI, MPN-SAF, and EORTC QLQ-C30
- Pearson correlations and analysis of variance/t-tests, multivariate regression models were used

RESULTS

- Insomnia is highly prevalent and severe
- Insomnia correlates with most other MPN-related symptoms and functional domains bearing a multi-faceted impact on overall quality of life.
- Cause of MPN-related sleep complaints is likely complex.
 - Emotional roots
 - Cognitive roots
 - Physical roots

Table 5: Multivariate analysis between insomnia and MPN-SAF items

	Pr> t
BFI Worst Fatigue	0.13
Early Satiety	0.12
Abdominal Pain	0.66
Abdominal Discomfort	0.22
Inactivity	0.22
Headaches	0.0001
Concentration	0.22
Dizziness/Vertigo/Lightheaded	0.24
Numbness/tingling	<0.0001
Depression/sad mood	<0.0001
Sexuality	0.006
Cough	0.09
Night sweats	<0.0001
Itching/pruritus	0.0042
Bone pain	0.07
Fever (>100 F)	0.01
Unintentional weight loss	0.75
Overall Quality of Life	.03



The Role of Sexuality Symptoms in Myeloproliferative Neoplasm Symptom Burden and Quality of Life: An Analysis by the MPN QOL International Study Group

Holly L. Geyer, MD¹; Björn Andersson, MD²; Heidi E. Kosloski, MS³; Amylou C. Duack, PhD⁴; Robyn M. Scherbar, MD, MPH⁵; Karl A. Martin, MD⁶; Kristina A. Butler, MD⁶; Claire N. Harrison, MD⁷; Deepak H. Radia, MD⁸; Francisco Cervantes, MD⁹; Jean-Jacques Kiladjian, MD, PhD¹⁰; Andreas Reiter, MD¹¹; Gunnar Birgegard, MD¹²; Francesco Passamonti, MD¹³; Zhenya Senyak¹⁴; Alessandro M. Vannucchi, MD¹⁵; Chiara Paoli, BS¹⁶; Zhijian Xiao, MD¹⁷; Jan Samuelsson, MD¹⁸; and Ruben A. Mesa, MD¹⁹

BACKGROUND: Patients with myeloproliferative neoplasms (MPNs) including polycythemia vera, essential thrombocythemia, and myelofibrosis, are faced with oppressive symptom profiles that compromise daily functioning and quality of life. Among these symptoms, sexuality-related symptoms have emerged as particularly prominent and largely unaddressed. In the current study, the authors evaluated how sexuality symptoms from MPN relate to other patient characteristics, disease features, treatments, and symptoms. **METHODS:** A total of 1971 patients with MPN (827 with essential thrombocythemia, 682 with polycythemia vera, 456 with myelofibrosis, and 6 classified as other) were prospectively evaluated and patient responses to the Myeloproliferative Neoplasm Symptom Assessment Form (MPN-SAF) and the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC-QLQ C30) were collected, along with information regarding individual disease characteristics and laboratory data. Sexuality scores were compared with an age-matched, healthy control population. **RESULTS:** Overall, patients with MPN were found to have greater sexual dysfunction compared with the healthy population (MPN-SAF score of 3.6 vs 2.0; $P<0.001$), with 64% of patients with MPN describing some degree of sexual dysfunction and 43% experiencing severe symptoms. The presence of sexual symptoms correlated closely with all domains of patient functionality (physical, social, cognitive, emotional, and role functioning) and were associated with a reduced quality of life. Sexual problems also were found to be associated with other MPN symptoms, particularly depression and nocturnal and microvascular-related symptoms. Sexual dysfunction was more severe in patients aged >65 years and in those with cytopenias and transfusion requirements, and those receiving certain therapies such as immunomodulators or steroids. **Conclusions:** The results of the current study identify the topic of sexuality as a prominent issue for the MPN population, and this area would appear to benefit from additional investigation and management. *Cancer* 2016;122:1888-96. © 2016 American Cancer Society

KEYWORDS: hematological neoplasms, myeloproliferative neoplasms, quality of life, sexuality, symptoms.

INTRODUCTION

Myeloproliferative neoplasms (MPNs) including essential thrombocythemia (ET), polycythemia vera (PV), and myelofibrosis (MF), are recognized for their severe symptom burden profiles. Constitutive catabolic and proliferative dysregulation results in a variety of secondary pathological effects including profound cytopenias, fatigue, thrombosis, cachexia,

Corresponding author: Ruben A. Mesa, MD, Department of Hematology/Oncology, Mayo Clinic, 13400 E. Shea Blvd, Scottsdale, AZ 85259; mesa.ruben@mayo.edu; and Holly Geyer, MD, Division of Hospital Internal Medicine, Mayo Clinic, 13400 E. Shea Blvd, Scottsdale, AZ 85259; geyer.holly@mayo.edu.

¹Division of Hospital Internal Medicine, Mayo Clinic, Scottsdale, Arizona; ²Internal Medicine, NU Hospital Organization, Uppsala, Sweden; ³Section of Biostatistics, Mayo Clinic, Scottsdale, Arizona; ⁴Department of Hematology and Oncology, Oregon Health and Science University, Portland, Oregon; ⁵Department of Psychiatry, Mayo Clinic, Scottsdale, Arizona; ⁶Department of Gynecology, Mayo Clinic, Scottsdale, Arizona; ⁷Department of Hematology, Guy's and St Thomas NHS Foundation Trust, London, United Kingdom; ⁸Hematology Department, Hospital Clinic, IDIBAPS, University of Barcelona, Barcelona, Spain; ⁹Clinical Investigation Centre Hospital Saint-Louis, Paris, France; ¹⁰Medical Clinic, University of Mannheim, Mannheim, Germany; ¹¹Department of Hematology, University Hospital, Uppsala, Sweden; ¹²Department of Hematology, IRCCS Foundation San Matteo Polylinic, University of Pavia, Pavia, Italy; ¹³MPN Forum, Asheville, North Carolina; ¹⁴Division of Hematology, Cicilio Hospital, Varese, Italy; ¹⁵Department of Medicine, University of Florence, Florence, Italy; ¹⁶MD5 and MPN Centre, Institute of Hematology and Blood Diseases Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Tianjin, China; ¹⁷Department of Internal Medicine, Stockholm South Hospital, Stockholm, Sweden; ¹⁸Division of Hematology/Oncology, Mayo Clinic, Scottsdale, Arizona

See editorial on page 1886-6, this issue.

We would like to thank the following contributors to the MPN QOL Subgroup: Stefanie Slot, Sonja Zwegman, Ana Kergulen Fuentes, Dolores Hernandez-Marquez, Konstanze Dohner, Pablo Musti, Carlos Besses, Peter L. Johansson, Alessandro Rambaldi, Tiziano Barbui, Karin Bonato, Francisco Boyer, Gabriel Blennay, Jean-Christophe Imort, Dana Renta, Lydia Roy, Jean-Yves Cahn, Norman Maldonado, Giovanni Barosi, Maria L. Ferrar, Robert Peter Gale, Yue Zhang, Zifeng Xu, Xiujun Sun, Junqing Xu, Peihong Zhang, Peter A.W. te Boekhorst, Harry Schouten, Hille L. Pahl, Martin Grieshammer, Frank Siegelmann, Thomas Lehmann, Keith Cannon, and Federico Sadrzangi.

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MPN Sexuality

- Included 1971 patients with MPN
- BFI, MPN-SAF, and EORTC-QLQ C30
- Pearson correlation and t-test models were used

- Sexuality correlated with all domains of patient functionality
- Close association between sexual symptoms and functional domains
- Symptom correlation with social and role functioning
- Likely multifactorial
 - Metabolic
 - Psychological

Correlation between sexuality problems and AF items	
	Pr> t
	0.33
	0.42
	0.42
	0.32
	0.04
	0.47
	0.06
	0.003
	0.20
	0.006
	0.0007
	0.035
	0.001
	0.73
	0.88
	0.80
	0.09
	<0.0001

Quality of Life: An Analysis by the



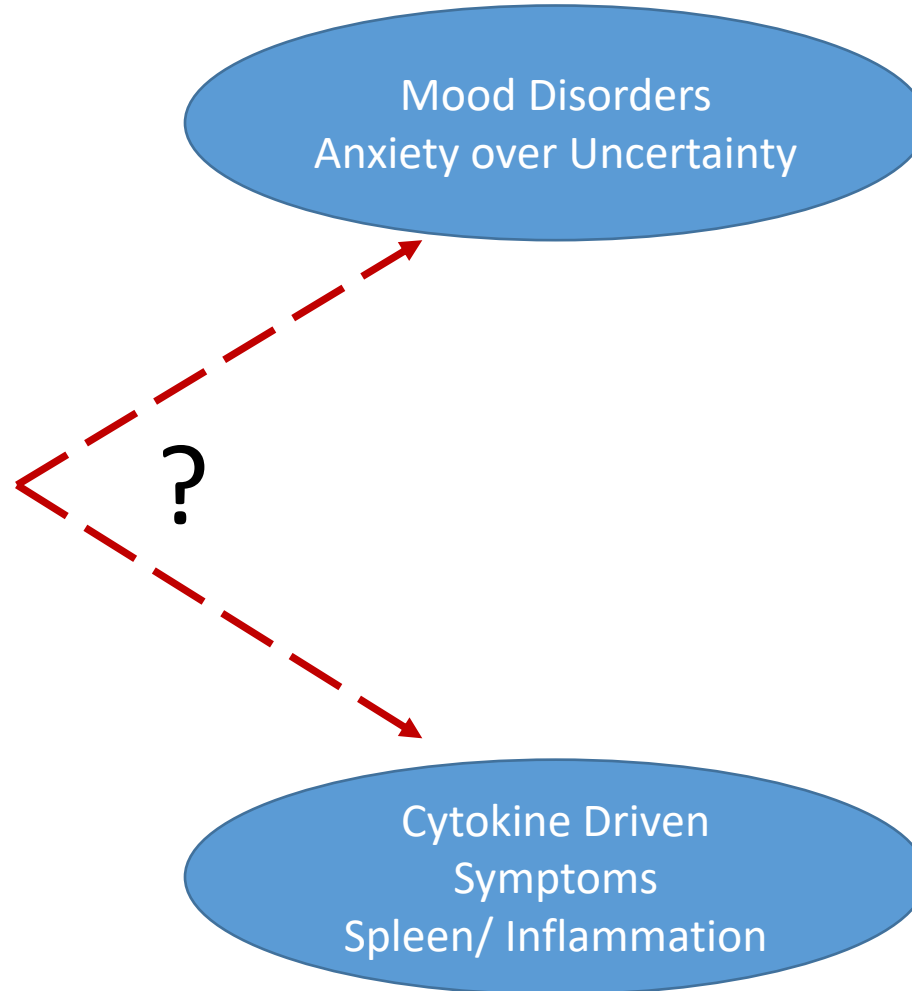
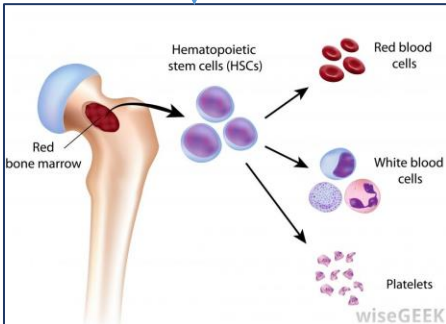
What Have MPN Patient Taught US?

1. Burden of having an MPN includes several clinical features including MPN associated symptoms
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What do symptoms tell us about MPN Biology?



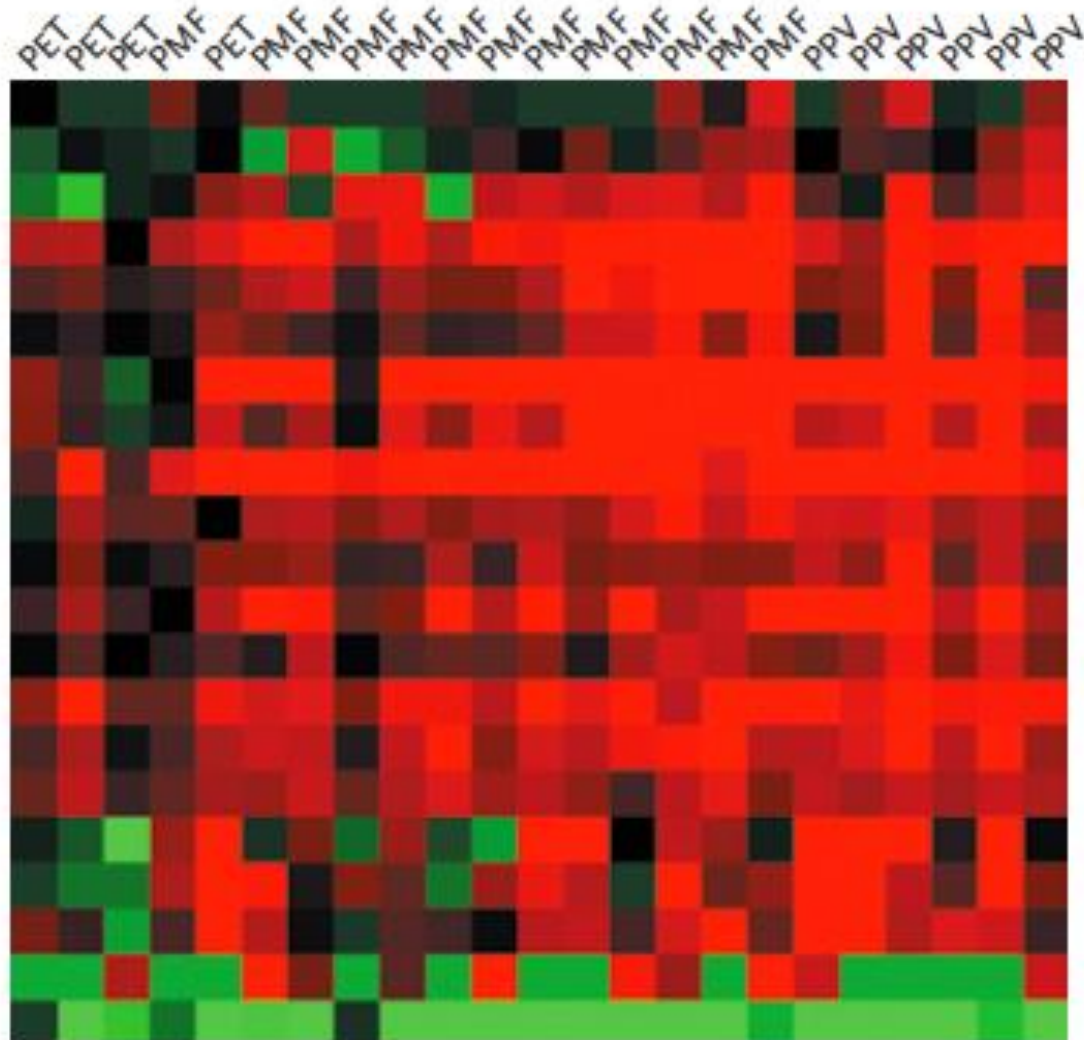
MPN
Symptoms



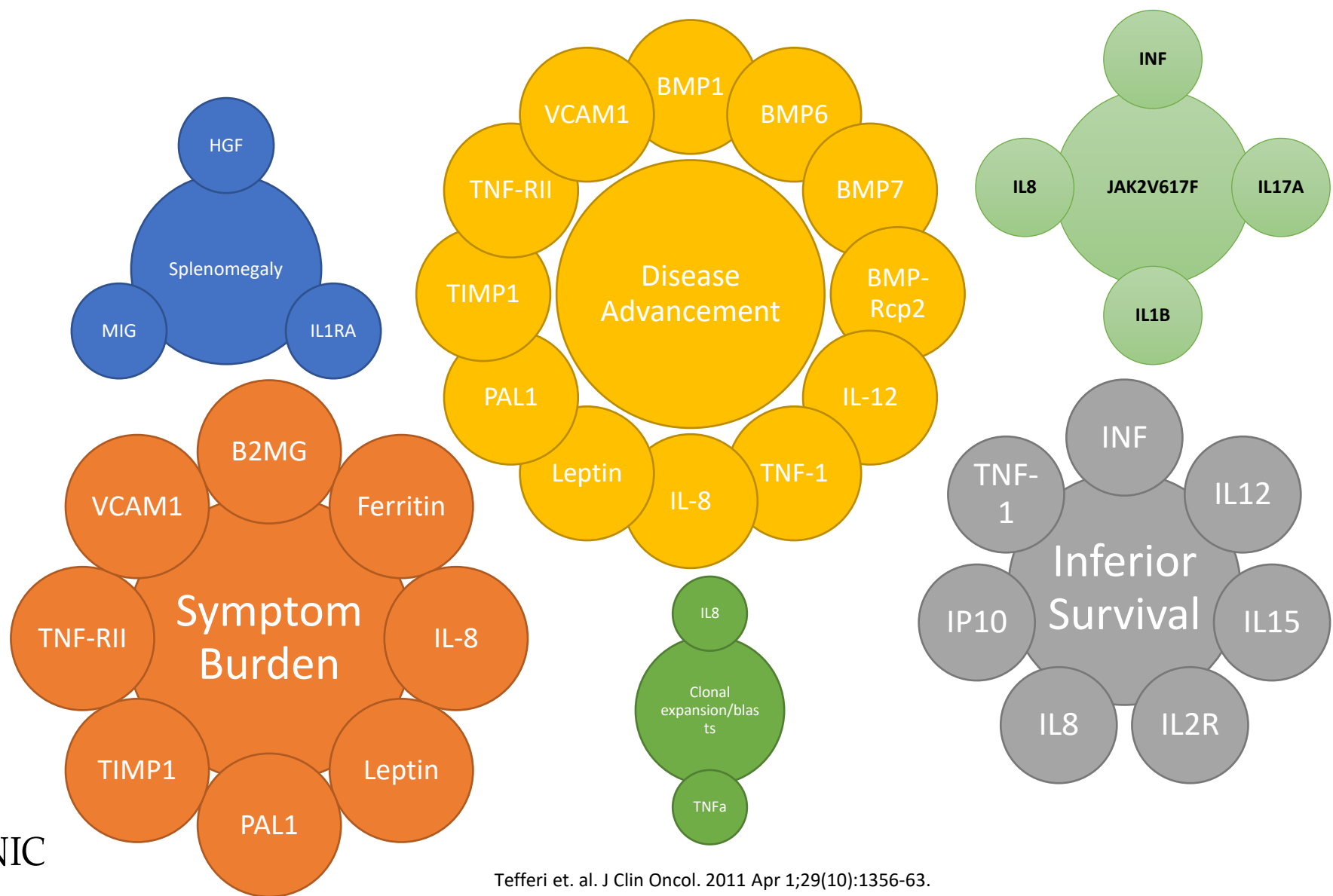
A Baseline, Patients with Myelofibrosis vs. Healthy Controls

V617F-

V617F+



Inflammatory Cytokines and Chemokines in the MPNs

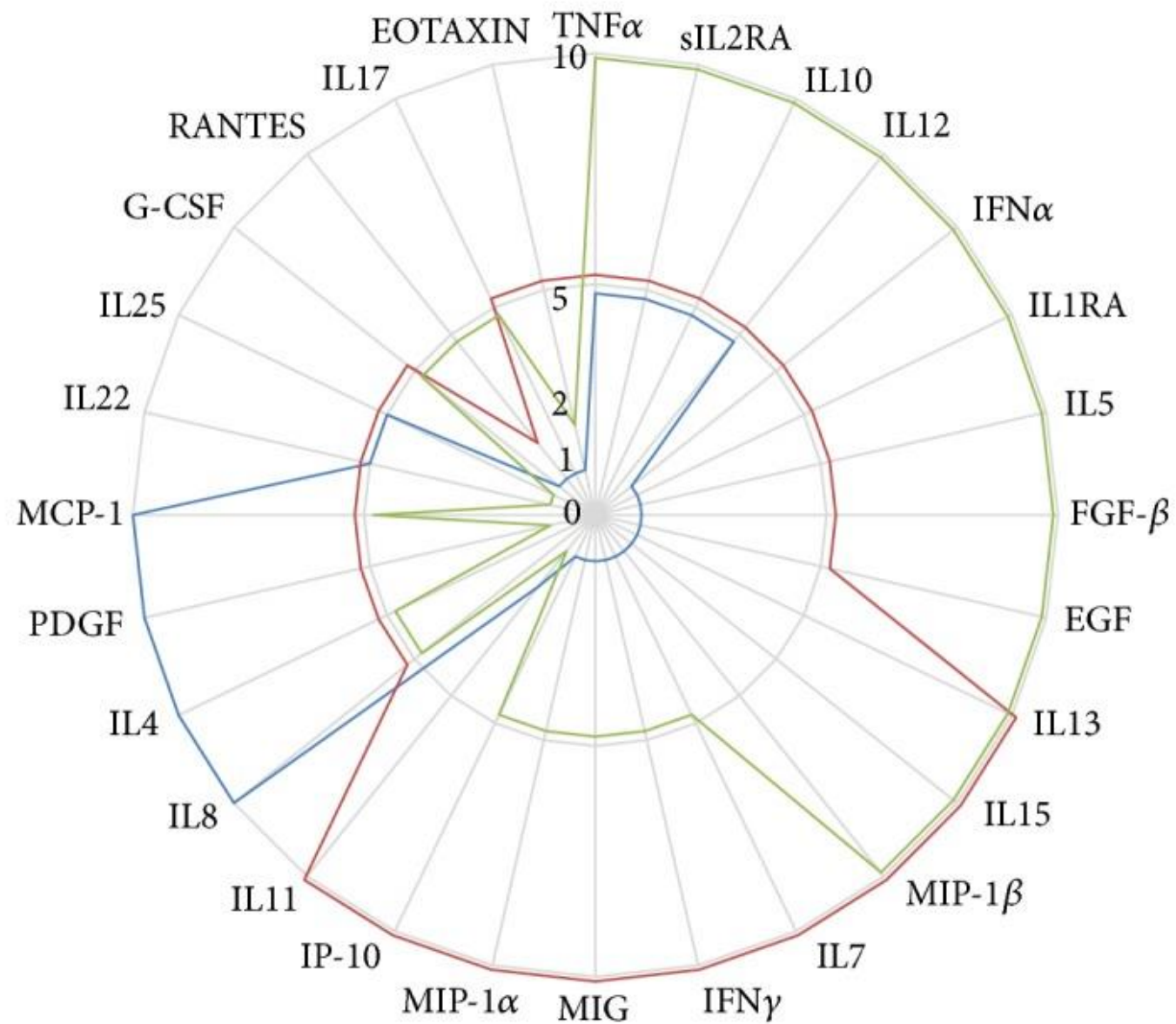


Tefferi et. al. J Clin Oncol. 2011 Apr 1;29(10):1356-63.
Geyer et. al. Mediators of Inflammation 2015. 1-9.

Cytokines & MPNs

Inflammatory marker*	Impact	Disorder
B2MICG	Symptoms	MF
BMP1	Disease advancement	PMF
BMP6	Disease advancement	PMF
BMP7	Disease advancement	PMF
BMP-Rcp2	Disease advancement	PMF
CD40L	Loss of appetite	MF
CRP	Thrombosis; atherogenesis	PV, ET
Ferritin	Pruritus	MF
FGF	Marrow fibrosis	PV, ET, PMF
HGF	Splenomegaly	PMF
IFN	Associated with JAK2V617F	MF
IL-12	Inferior survival; transfusion requirements, vascular complications	MF
IL-15	Inferior survival	MF
IL-17A	Associated with JAK2V617F	MF
IL-1B	Associated with JAK2V617F	MF
IL-1RA	Splenomegaly	PMF
IL-2R	Inferior survival; transfusion requirements	MF
IL-8	Elevated blasts; constitutional symptoms	MF
IL-8	Associated with JAK2V617F	MF
IP-10	Inferior survival	MF
LEPTIN	Symptoms; weight loss	MF
MIG	Splenomegaly	PMF
PAL1	Insomnia	MF
PTX	Thrombosis; atherogenesis	PV, ET
RANTES	Insomnia	MF
TIMP1	Symptoms	MF
TNF-1	Clonal expansion	JAK2V617F+ MPNs
TNFR1I	Symptoms	MF
VCAM1	Symptoms	MF
VEGFb	Marrow fibrosis	PV, ET, PMF

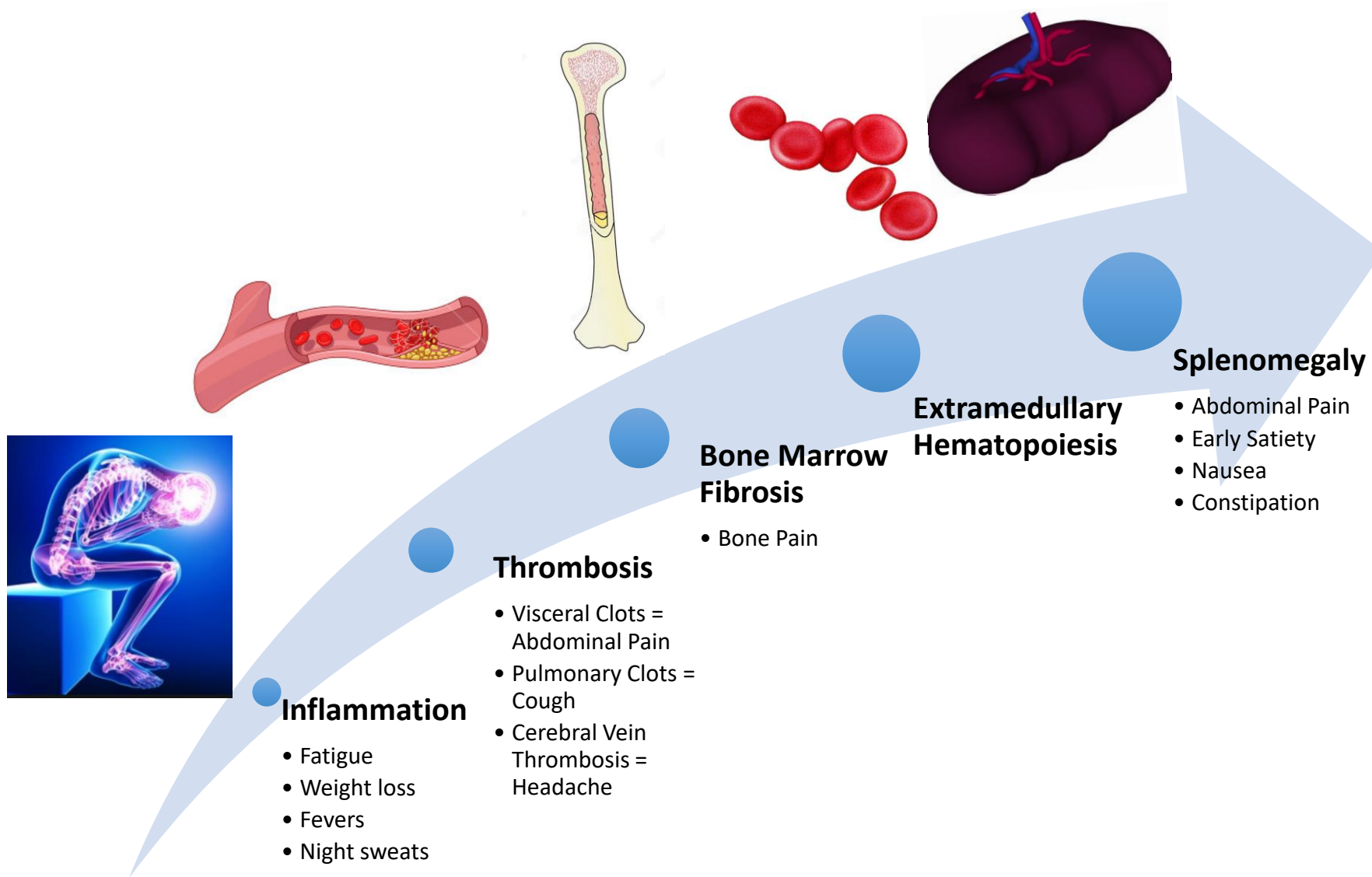
Geyer et. al. 2015
Mediators of Inflammation



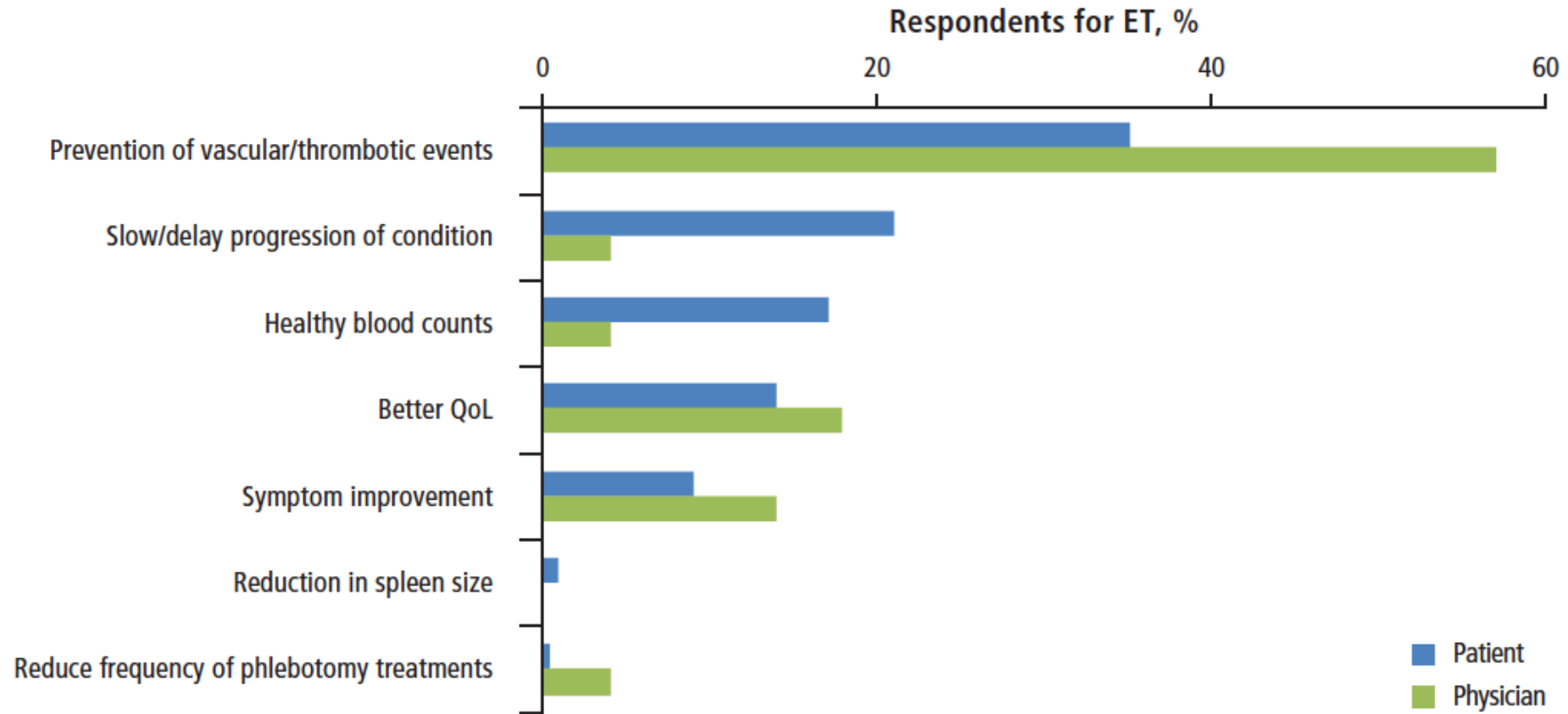
— Essential thrombocythemia
 — Polycythemia vera
 — Primary myelofibrosis

Mondet et. al.
 Mediators of Inflammation 2015

The Sequelae of Inflammation in MPNs



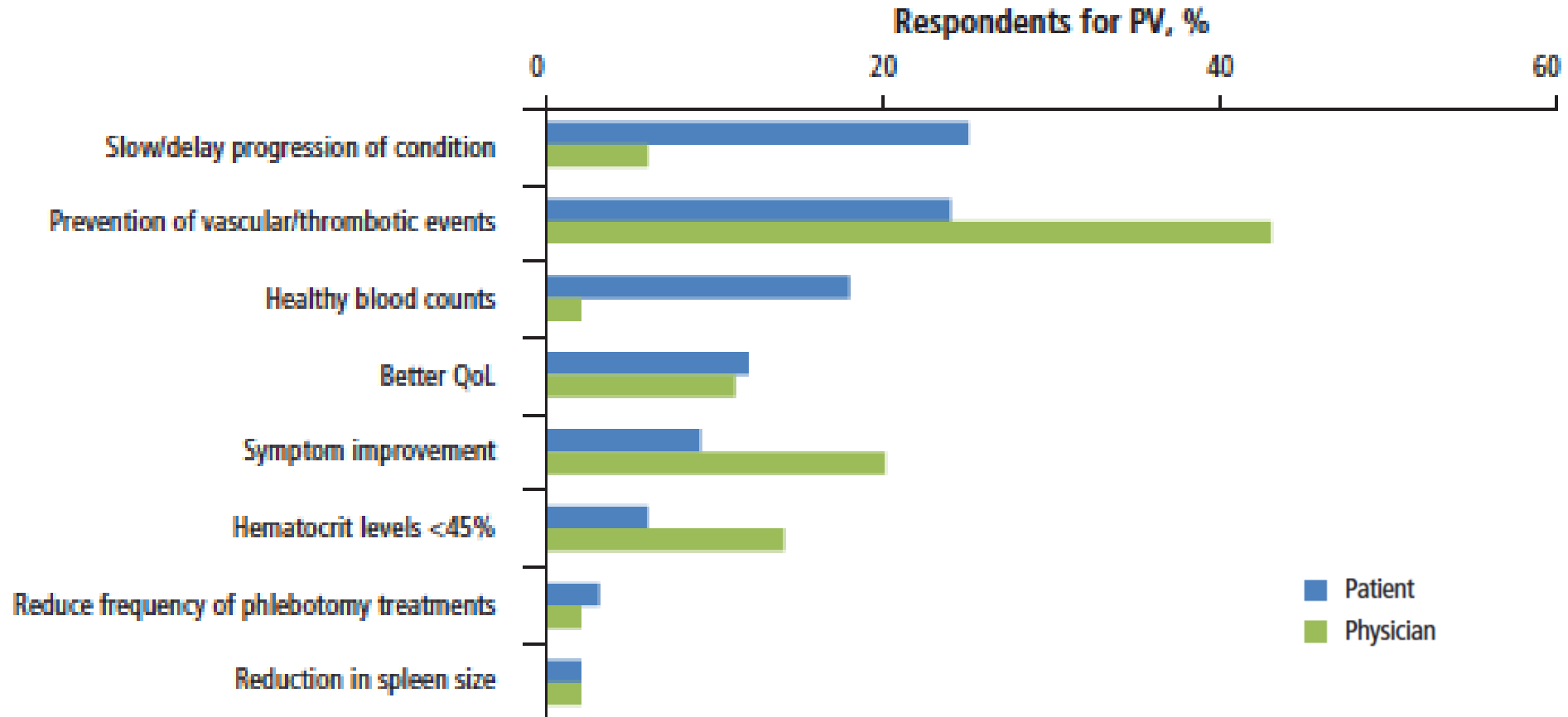
LANDMARK Study in ET Goals (Patients (N=226) & Physicians)



Mesa et. al.
BMC Cancer
2016;16:167

LANDMARK Study in PV

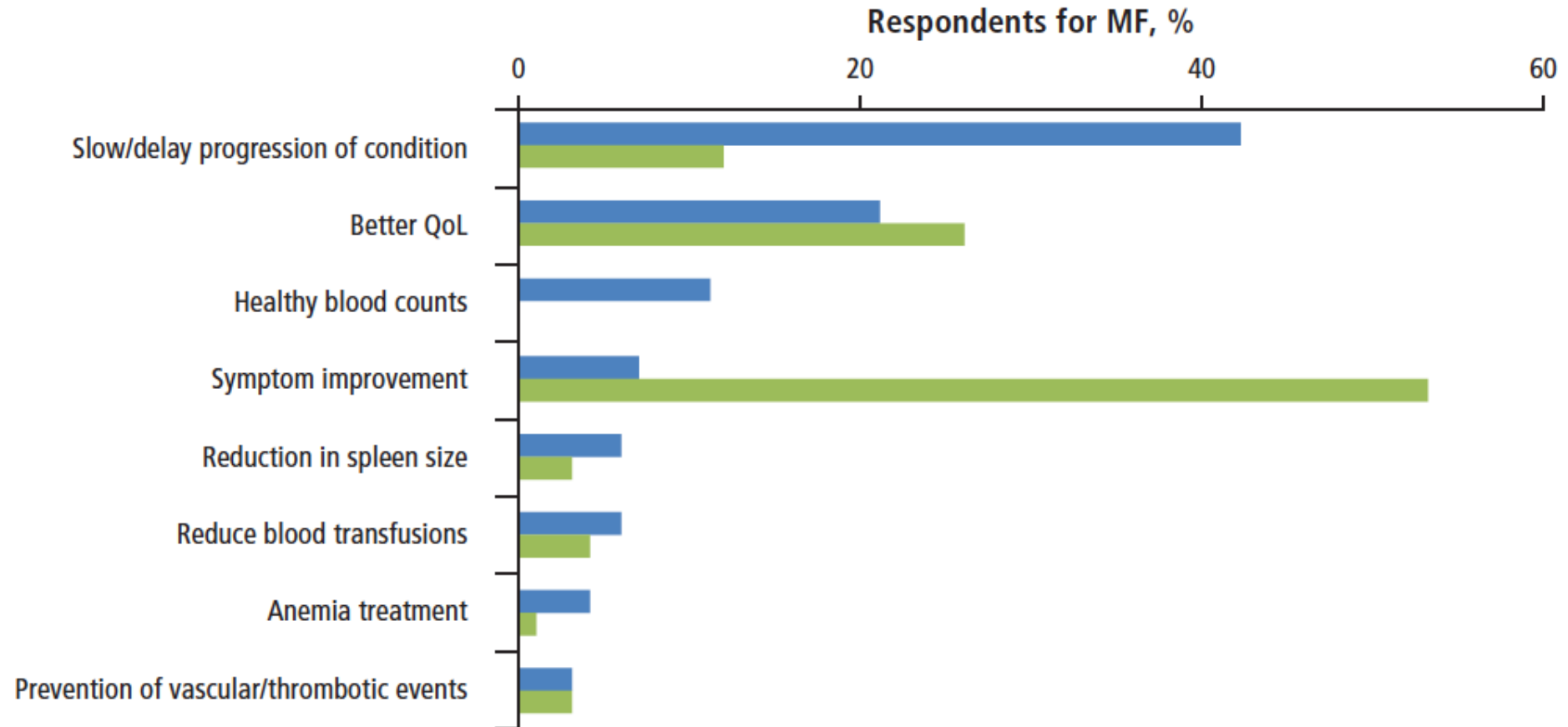
Goals (Patients (N=382) & Physicians)



Mesa et. al.
BMC Cancer
2016;16:167

LANDMARK Study in MF

Goals (Patients (N=207) & Physicians)



Mesa et. al.
BMC Cancer
2016;16:167

MF Patient vs physician-reported most important goal for therapy

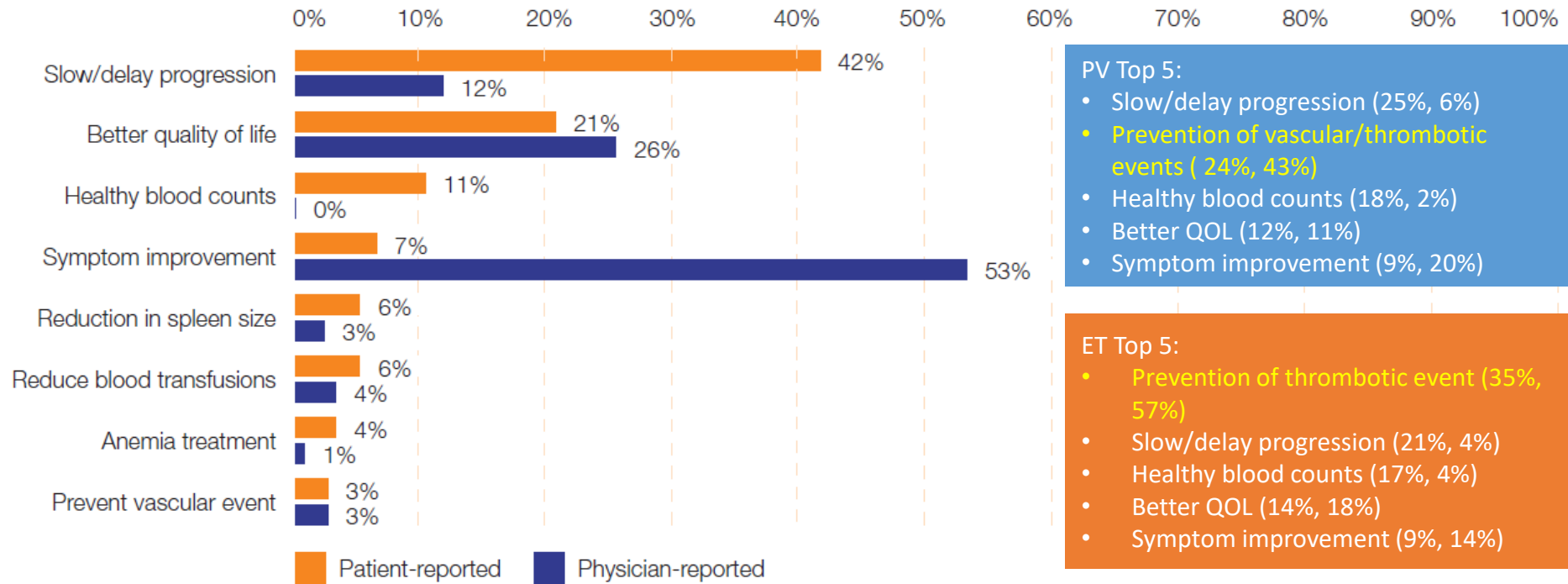
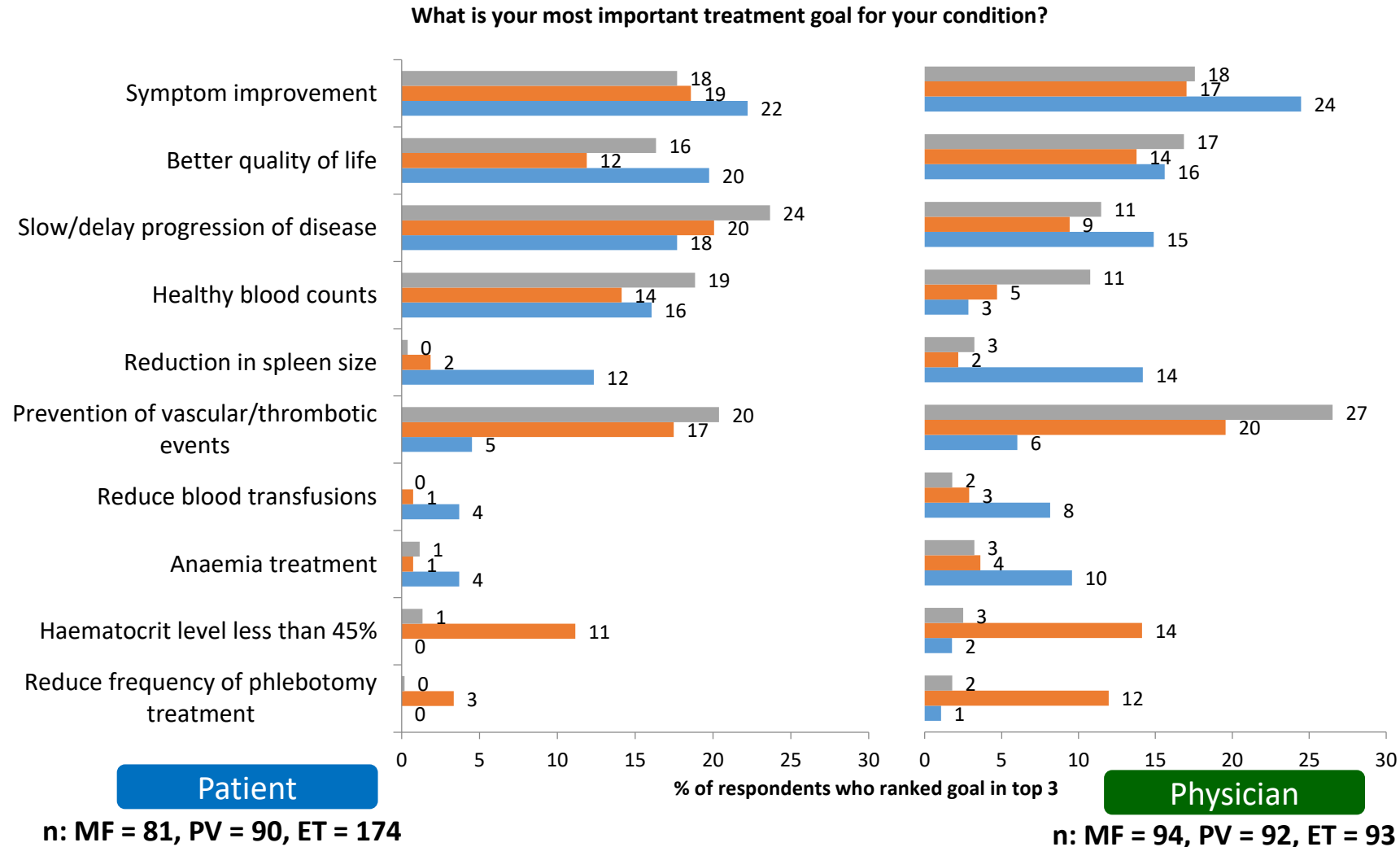


Figure 55. Question 32: Other than a cure for diagnosis, what is your most important treatment goal for therapy? (n = 207)

Question 36: Other than a cure for this diagnosis, what is your most important treatment goal for therapy? (n = 156)

Treatment goals - Patients vs. Physicians view (Q36 + Q31)

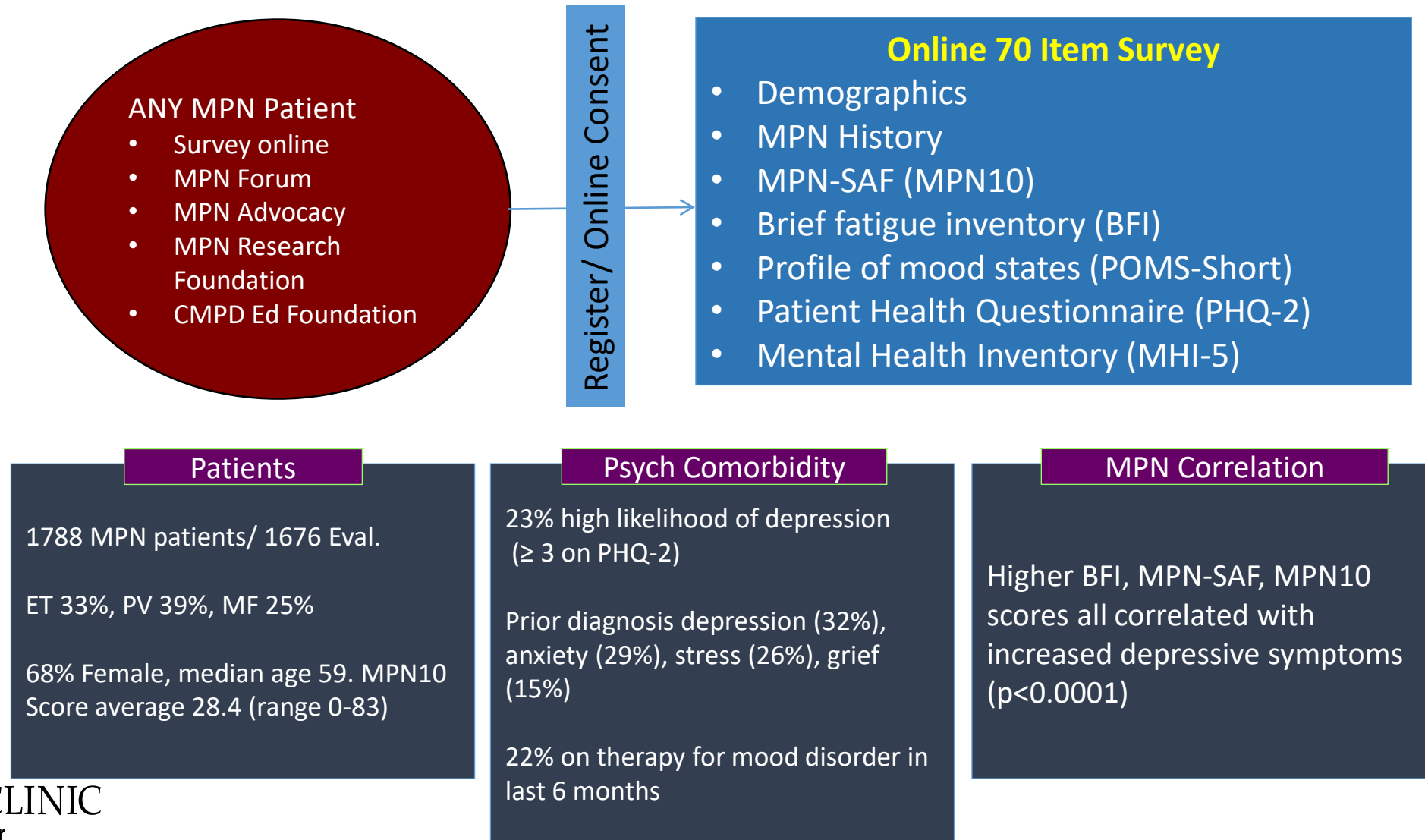
ET and PV patients wish to slow disease progression whilst physicians are more concerned about thrombotic events. In all diseases both Patients & Physicians look for symptom improvements



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Collaborative Internet Based Trial with MPN Forum



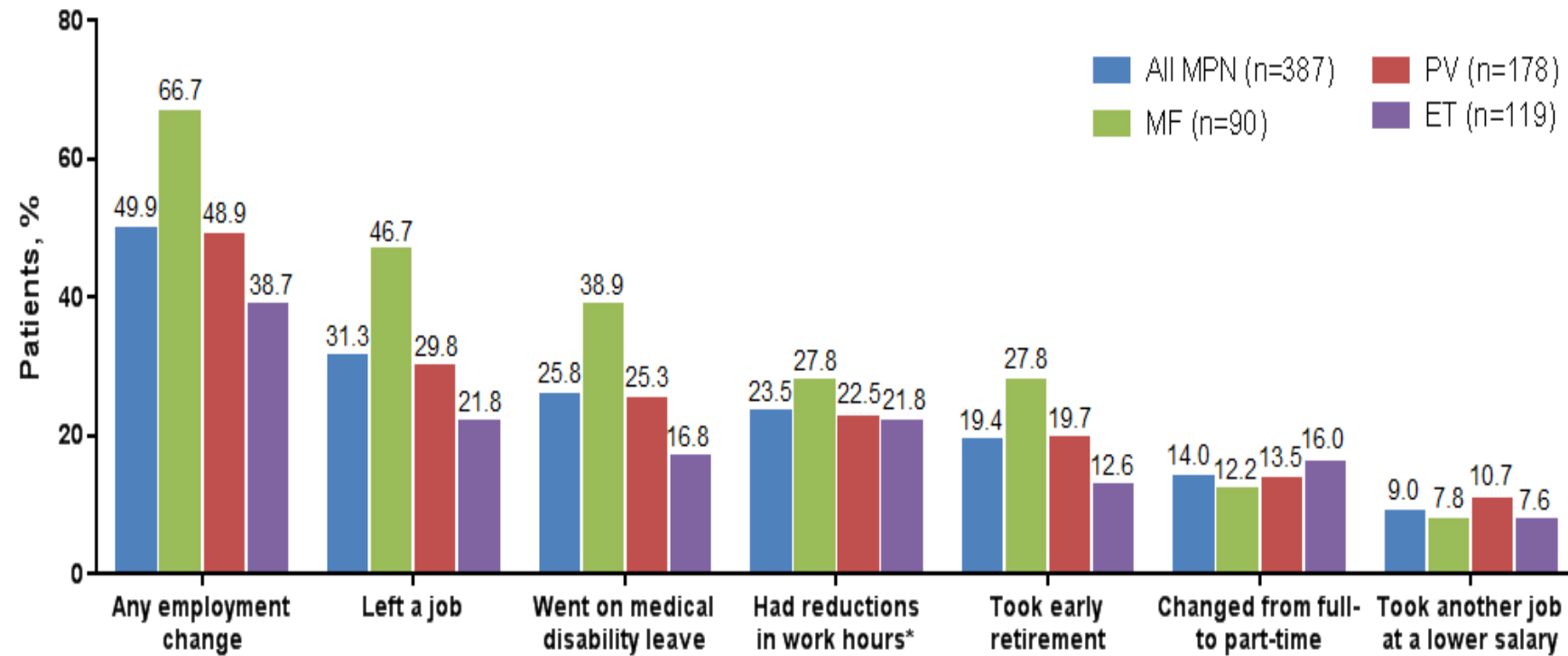
Item	PHQ ≥ 3 (high likelihood of depression)	PHQ < 3 (low likelihood of depression)
MPN-SAF items and scoring		
MPN-TSS (MPN-10, mean score)*	41.1 (16.7)	24.7 (15.9)
Brief Fatigue Inventory (BFI)*	6.3 (1.7)	3.8 (2.3)
Worst Fatigue (last 24-hours)*	7.8 (1.9)	5.8 (2.7)
Early Satiety*	4.1 (3.1)	2.5 (2.8)
Abdominal pain*	2.8 (3.1)	1.4 (2.2)
Abdominal discomfort*	3.6 (3.1)	2.1 (2.5)
Inactivity*	5.6 (2.6)	2.8 (2.7)
Headache*	3.8 (3.3)	2.2 (2.7)
Concentration difficulties*	6.1 (2.6)	3.4 (2.9)
Dizziness*	4.2 (3.3)	2.3 (2.6)
Numbness*	3.8 (3.3)	2.7 (3.0)
Insomnia*	5.4 (3.3)	3.7 (3.0)
Sad mood*	6.2 (2.3)	2.4 (2.4)
Sexual difficulties*	6.2 (3.4)	3.7 (3.4)
Cough*	2.9 (3.1)	1.5 (2.4)
Night sweats*	4.0 (3.5)	2.4 (2.9)
Pruritus*	3.8 (3.5)	2.5 (2.9)
Bone Pain*	3.9 (3.6)	2.2 (2.9)
Fever*	0.7 (1.8)	0.2 (1.1)
Weight loss*	1.5 (2.7)	0.8 (2.0)
Overall quality of life (QOL)*	5.8 (2.1)	3.1 (2.2)
Mental Health Inventory Score*	16.5 (4.3)	23.3 (3.9)
POMS-B Subscales		
Tension-anxiety*	11.5 (4.0)	16.2 (3.2)
Vigor-activity*	3.3 (3.0)	6.8 (4.4)
Fatigue-inertia*	5.3 (3.9)	11.2 (5.1)
Depression-dejection*	10.6 (4.4)	17.0 (3.1)
Confusion-bewilderment*	11.2 (4.0)	15.2 (3.0)
Anger-hostility*	12.6 (4.6)	16.7 (3.3)
POMS-B total score*	54.6 (16.0)	83.2 (16.0)

Mood and MPNs 1788 MPN Patients

- MPN-SAF
- PHQ3, POMS-B
- *MPN10 and every Symptom higher with Depression*
- *Depression not linked to MF, PV or ET risk scores*

Scherber et. al. ASH 2016

Employment change due to MPNs



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MPN Recent Phase III Trials

MPN Symptom Assessment

Disease	Drug	MPN Symptom Tool
MF	RUXO (COMFORT 1)	MF-SAF 2.0
MF	RUXO (COMFORT 2)	FACT-LYM
MF	Fedratinib (JAKARTA)	MF-SAF
MF	Pacritinib (PERSIST 1&2)	MPN-SAF
MF	Momelotinib (SIMPLIFY 1&2)	MPN-SAF
MF	Pomalidomide (RESUME)	FACT-AN
MF	RUXO (RETHINK)	MPN-10
PV	Ruxo (RESPONSE)	MPN-SAF
PV	Ruxo (RELIEF)	MPN-SAF
PV	PEG INFa2a (MPD-RC 112)	MPN-SAF
ET	Ruxo (MAGIC)	MPN-SAF
ET	PEG INFa2a (MPD-RC 112)	MPN-SAF



National
Comprehensive
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Network®

NCCN Guidelines Version 1.2017 Panel Members

Myeloproliferative Neoplasms

Ruben Mesa, MD/Chair
Mayo Clinic Cancer Center

Catriona Jamieson, MD, PhD/Vice-Chair
UC San Diego Moores Cancer Center

Ravi Bhatia, MD
University of Alabama at Birmingham
Comprehensive Cancer Center

Michael W. Deininger, MD, PhD
Huntsman Cancer Institute at the
University of Utah

Aaron T. Gerds, MD, MS
Case Comprehensive Cancer Center/
University Hospitals Seidman Cancer
Center and Cleveland Clinic Taussig
Cancer Institute

Ivana Gojo, MD
The Sidney Kimmel Comprehensive
Cancer Center at Johns Hopkins

Jason Gotlib, MD, MS
Stanford Cancer Institute

Krishna Gundabolu, MBBS
Fred & Pamela Buffett Cancer Center

Gabriela Hobbs, MD
Massachusetts General Hospital
Cancer Center

Rebecca B. Klisovic, MD
The Ohio State University Comprehensive
Cancer Center - James Cancer Hospital
and Solove Research Institute

Patricia Kropf, MD
Fox Chase Cancer Center

Sanjay R. Mohan, MD
Vanderbilt-Ingram Cancer Center

Marie Huong Nguyen, MD
University of Michigan
Comprehensive Cancer Center

Stephen Oh, MD, PhD
Siteman Cancer Center at Barnes-
Jewish Hospital and Washington
University School of Medicine

Eric Padron, MD
Moffitt Cancer Center

Nikolai Podoltsev, MD, PhD
Yale Cancer Center/
Smilow Cancer Hospital

Daniel A. Pollyea, MD, MS
University of Colorado Cancer Center

Raajit Rampal, MD, PhD
Memorial Sloan Kettering Cancer Center

Lindsay A. M. Rein, MD
Duke Cancer Institute

Bart Scott, MD, MS
Fred Hutchinson Cancer Research Center/
Seattle Cancer Care Alliance

David S. Snyder, MD
City of Hope Comprehensive Cancer Center

Brady L. Stein, MD, MHS
Robert H. Lurie Comprehensive Cancer Center of
Northwestern University

Srdan Verstovsek, MD, PhD
The University of Texas
MD Anderson Cancer Center

Martha Wadleigh, MD
Dana-Farber/Brigham and Women's
Cancer Center

Eunice S. Wang, MD
Roswell Park Cancer Institute



NCCN Guidelines Version 1.2017

Myeloproliferative Neoplasms

MYELOPROLIFERATIVE NEOPLASM SYMPTOM ASSESSMENT FORM TOTAL SYMPTOM SCORE (MPN-SAF TSS-10 ITEMS)

(Recommended for monitoring symptoms during the course of treatment)

Circle the one number that describes how, during the past week how much difficulty you have had with each of the following symptoms

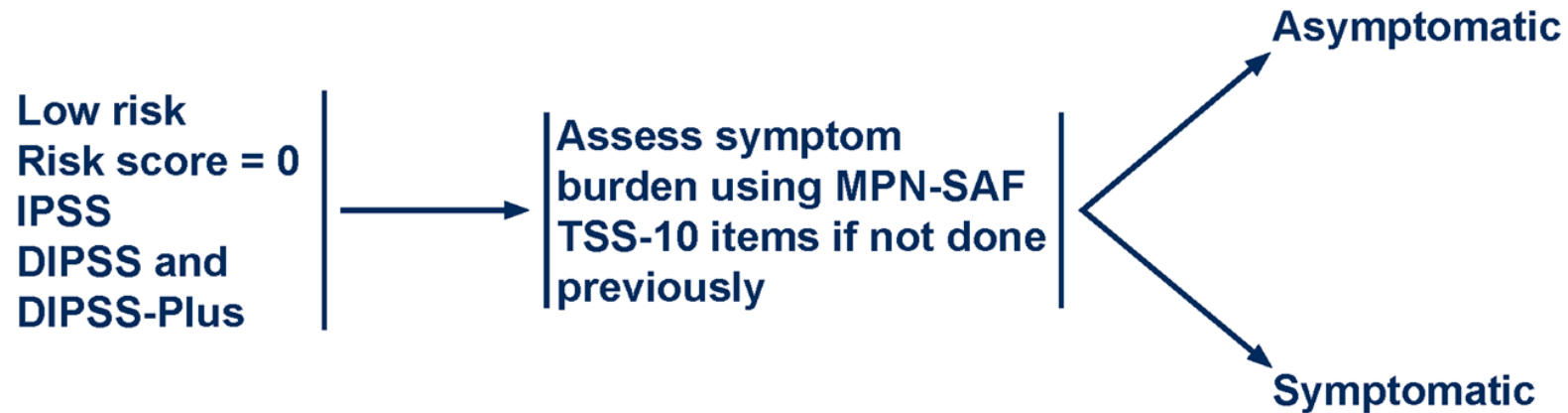
Filling up quickly when you eat (early satiety)	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
Abdominal discomfort	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
Inactivity	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
Problems with concentration-compared to prior to my MPD	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
Numbness/Tingling (in my hands and feet)	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
Night sweats	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
Itching (pruritus)	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
Bone pain (diffuse not joint pain or arthritis)	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
Fever (>100 F)	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Daily)
Unintentional weight loss last 6 months	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)

MPN-C
3 OF 3



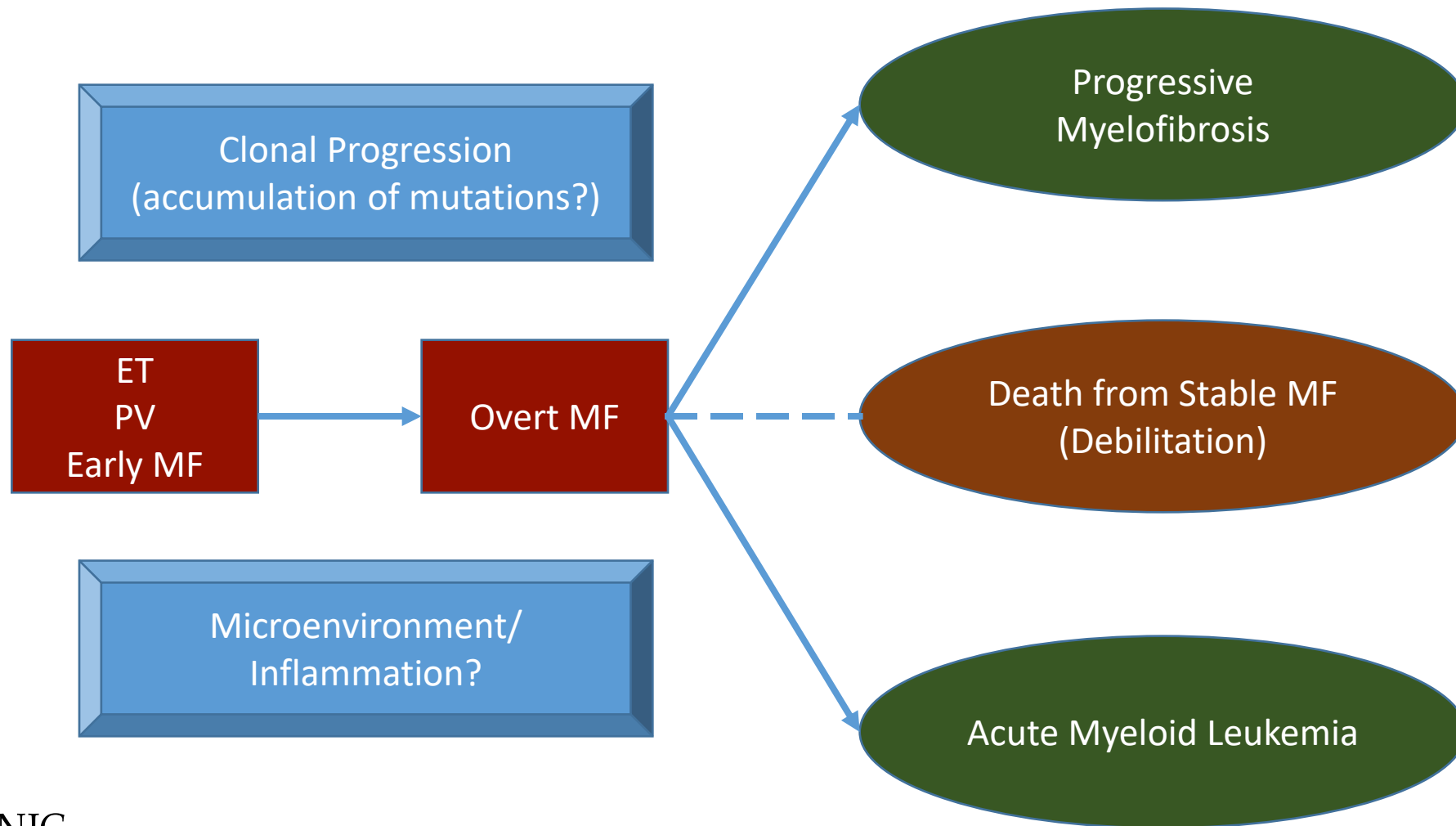
NCCN Guidelines Version 1.2017 Myeloproliferative Neoplasms

TREATMENT FOR LOW-RISK MYELOFIBROSIS



MPN-2

Why do MPNs Progress?

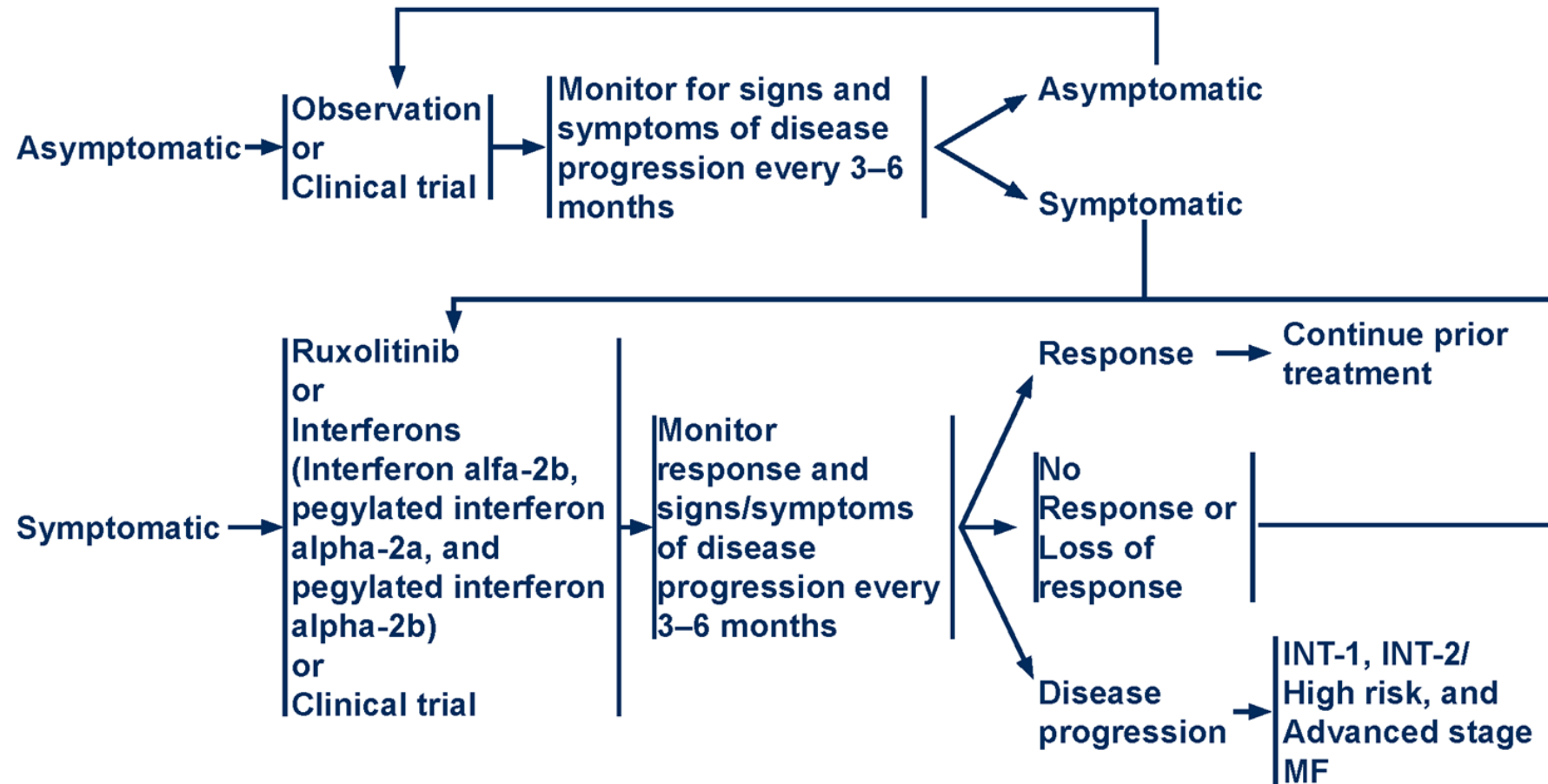




NCCN Guidelines Version 1.2017

Myeloproliferative Neoplasms

TREATMENT FOR LOW-RISK MYELOFIBROSIS



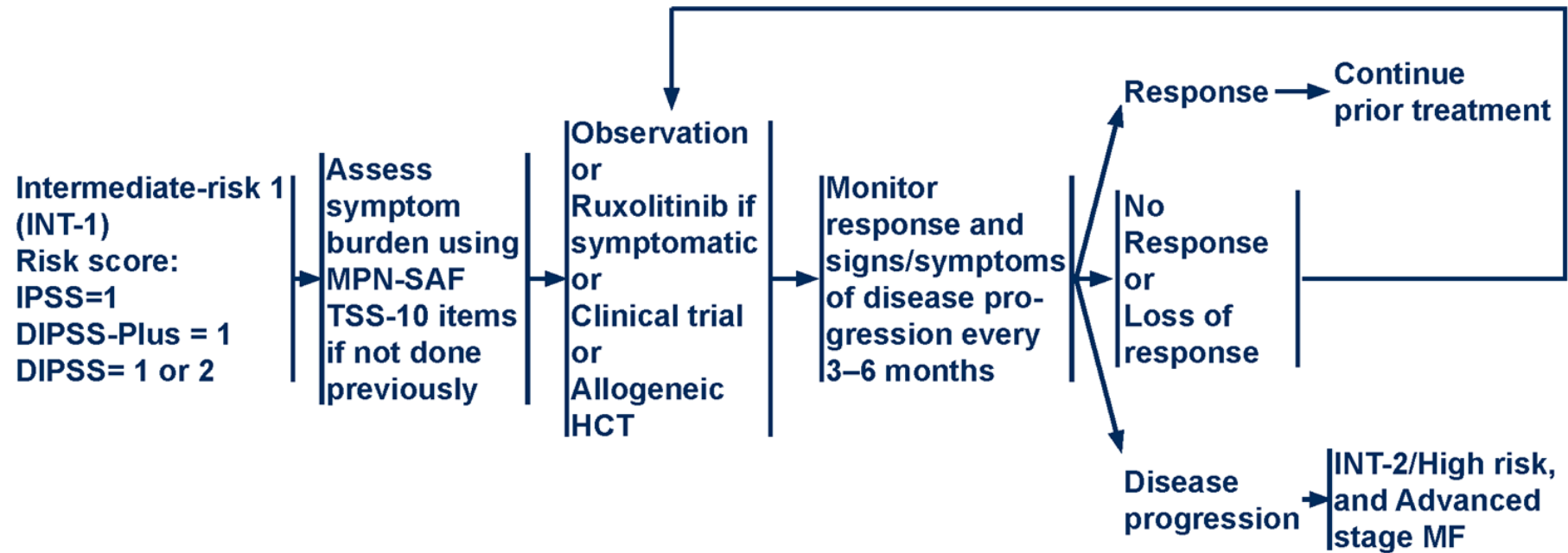
MPN-2



NCCN Guidelines Version 1.2017

Myeloproliferative Neoplasms

TREATMENT FOR INTERMEDIATE-RISK 1 (INT-1) MYELOFIBROSIS

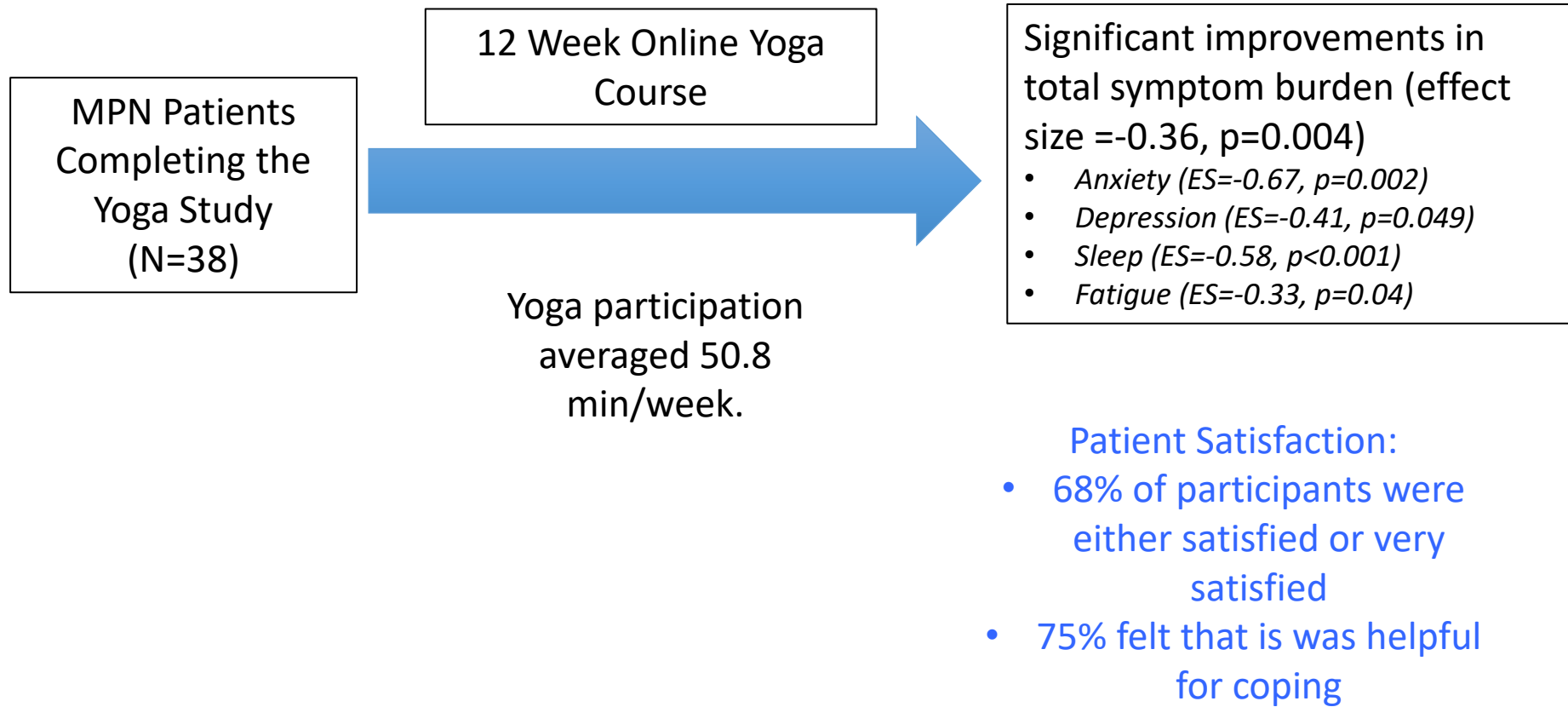


MPN-3

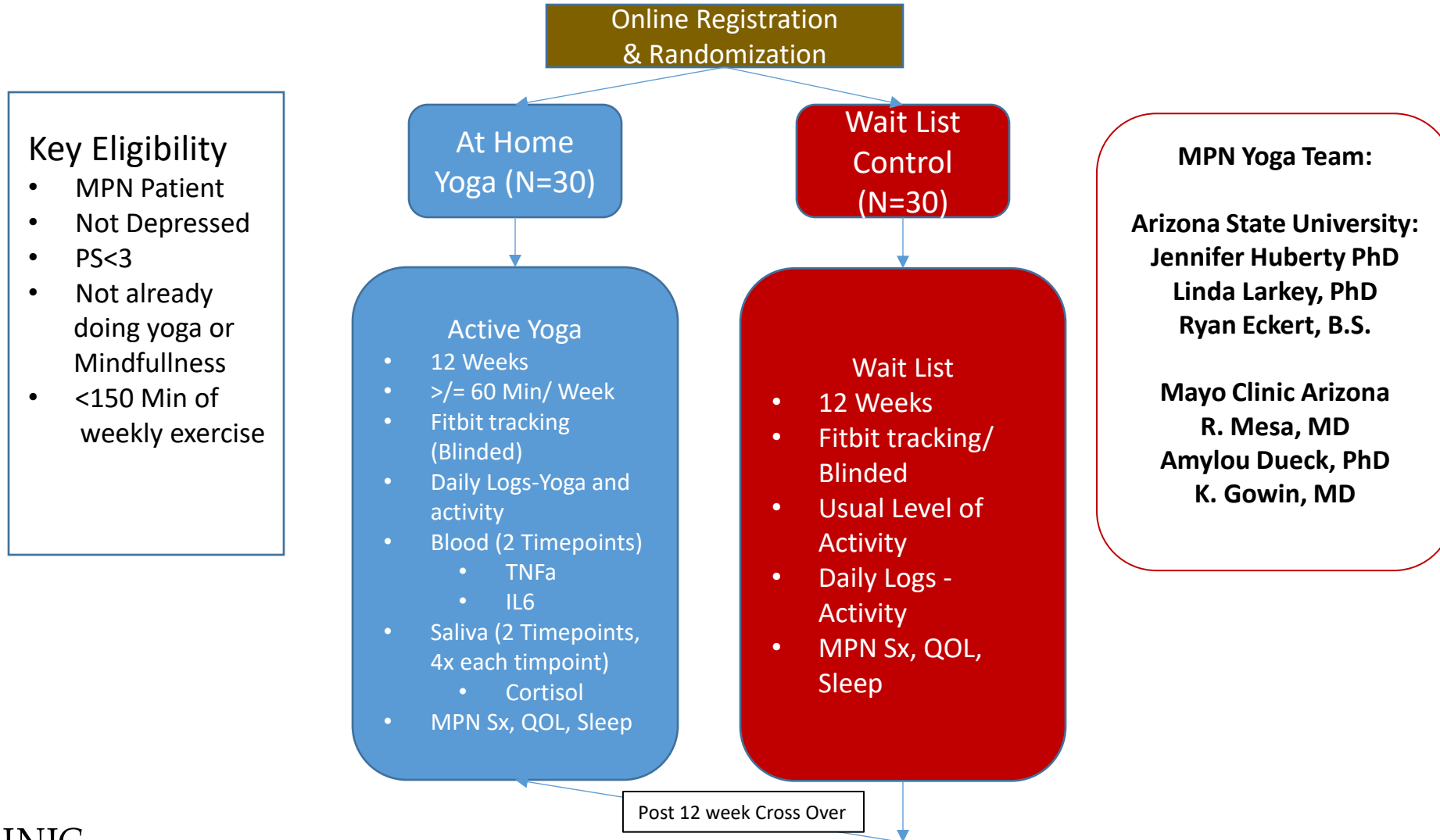
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Non-Pharmacologic Approaches in the MPNs: Online-Streamed Yoga

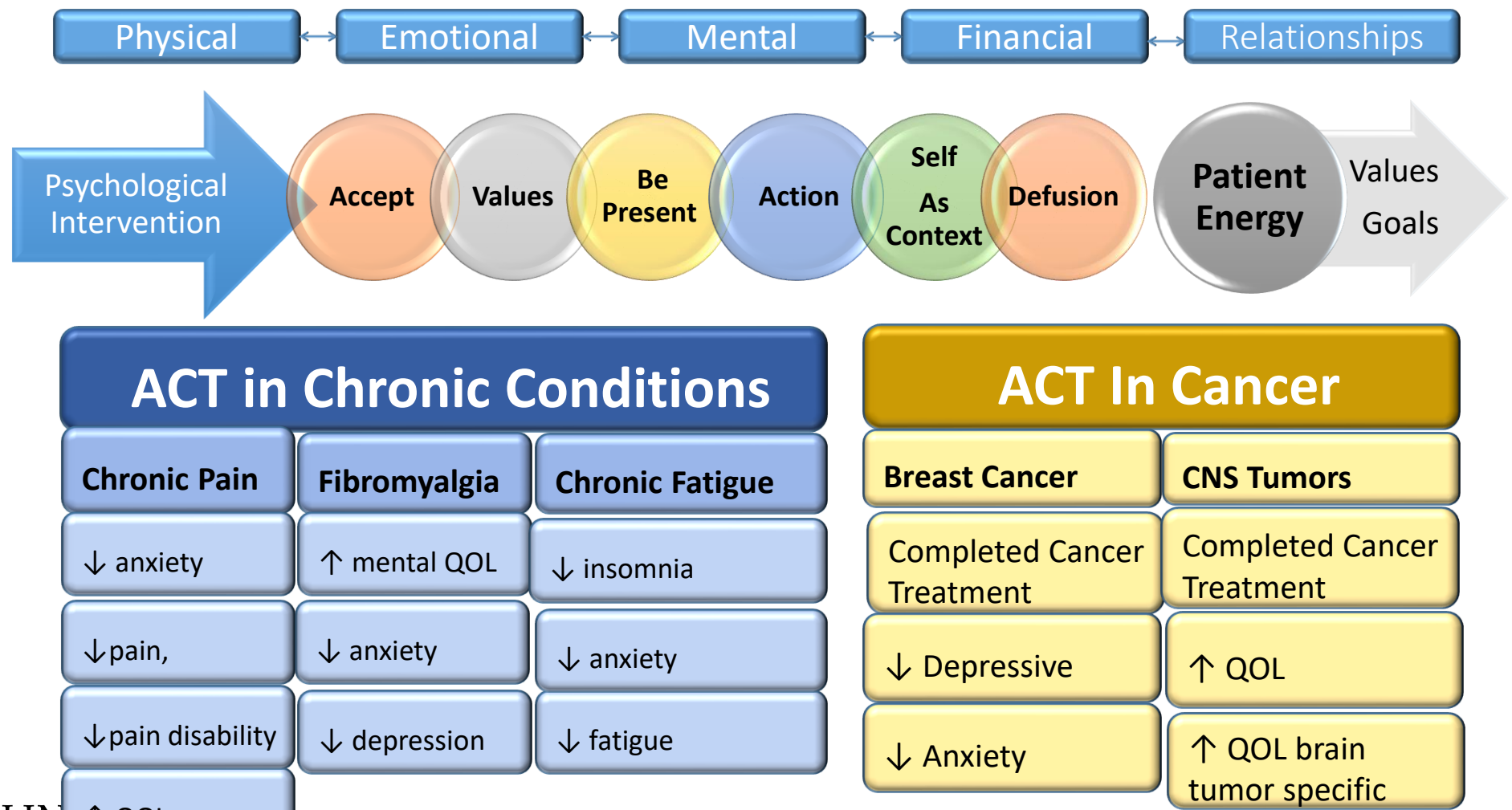


MPN Yoga II - Pilot



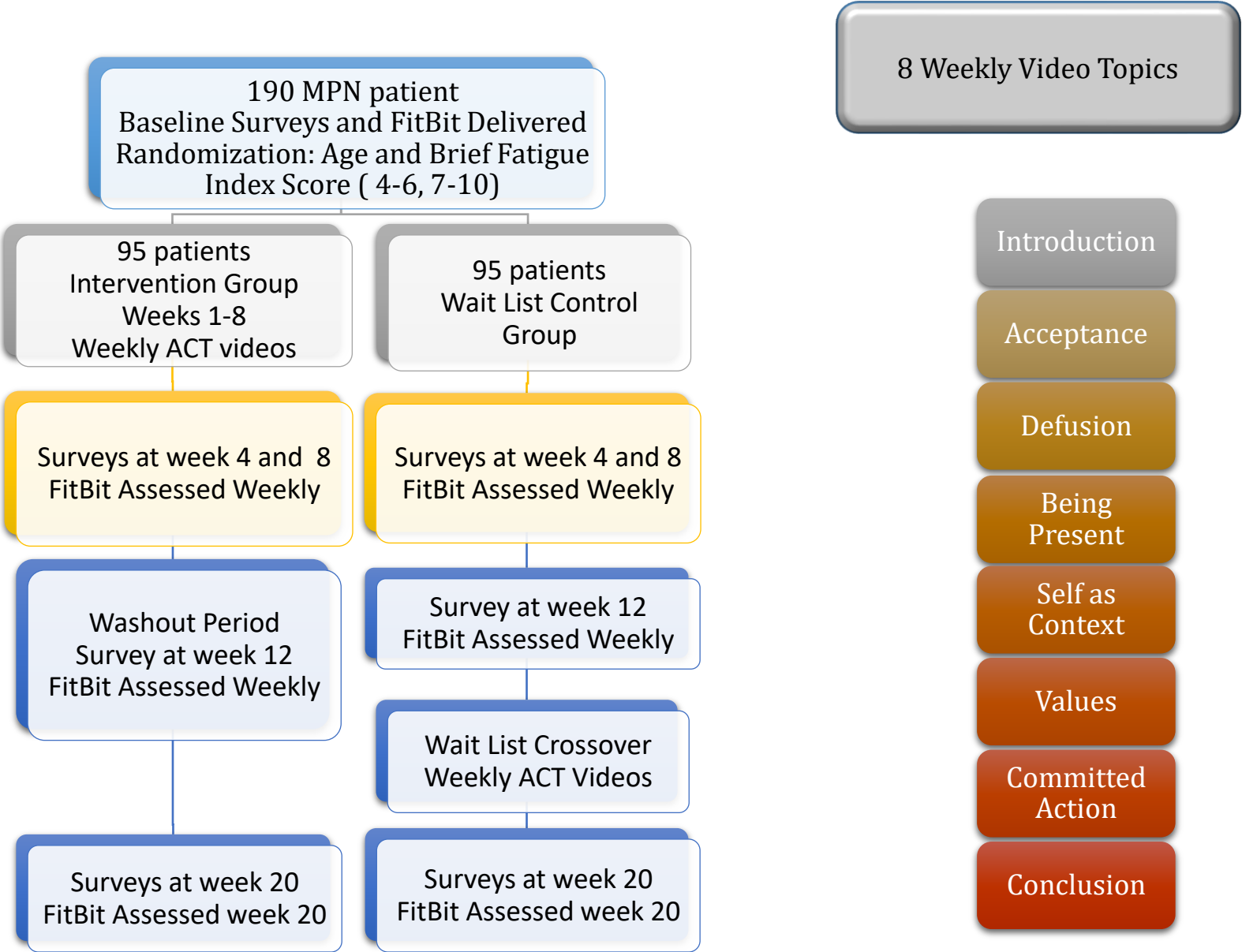
Acceptance and Commitment Therapy for MPNs

-The Opportunity-



Non-Pharmacologic Approaches in the MPNs:

MyACT Study: Video Intervention to reduce fatigue

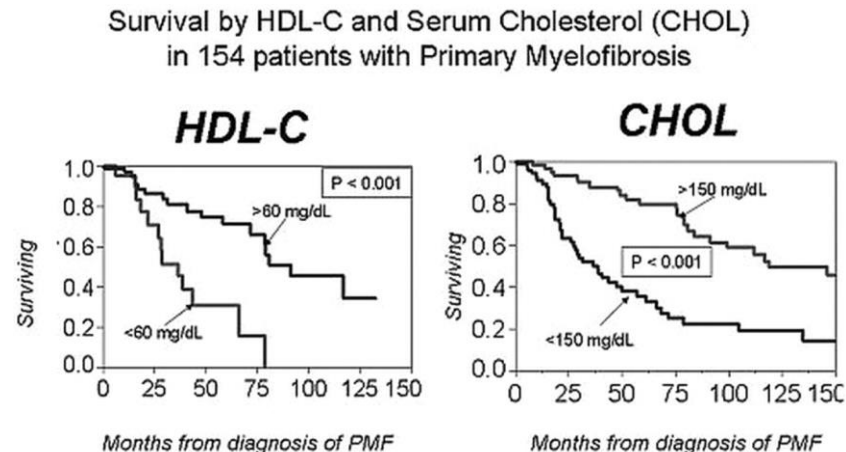


What about diet?

- Diets which emphasize anti-inflammatory properties:
- Reduce CRP ($p = 0.015$) and IL-6 levels ($p = 0.025$).
- Improve thrombotic markers
 - Decrease in homocysteine levels ($p = 0.031$)
 - Decreased white blood cell counts ($p = 0.001$)
 - Normalization of fibrinogen levels ($p = 0.025$).
- Anti-inflammatory diets have demonstrated good efficacy when utilized in nutritional intervention for high-inflammation disease states such inflammatory bowel disease.
 - In an intervention among patients with IBD ($N=40$), 60% had “good” or “very good” response in IBD severity after four weeks of dietary compliance
 - Of note, $JAK2^{V617F}$ mutations exceeded expected thresholds for IBD patients expressing thrombocytosis (23%) or erythrocytosis (10%).
- *To date, no dietary interventions have been evaluated in MPN patients.*

Nutrition in the MPNs

- 13% of MPN patients endorse undesired weight loss
 - MF 20% followed by PV (10%) and ET (7%)
- Analysis of the Mayo database:
 - 67% of MF patients lost weight over time
 - 27% of patients had decreased BMI category
- Patients with MPN are more likely to be deficient in LDL-C and total cholesterol compared to age-matched controls
- Hypcholesterolemia is independently associated with decreased survival PMF patients ($p < 0.001$)



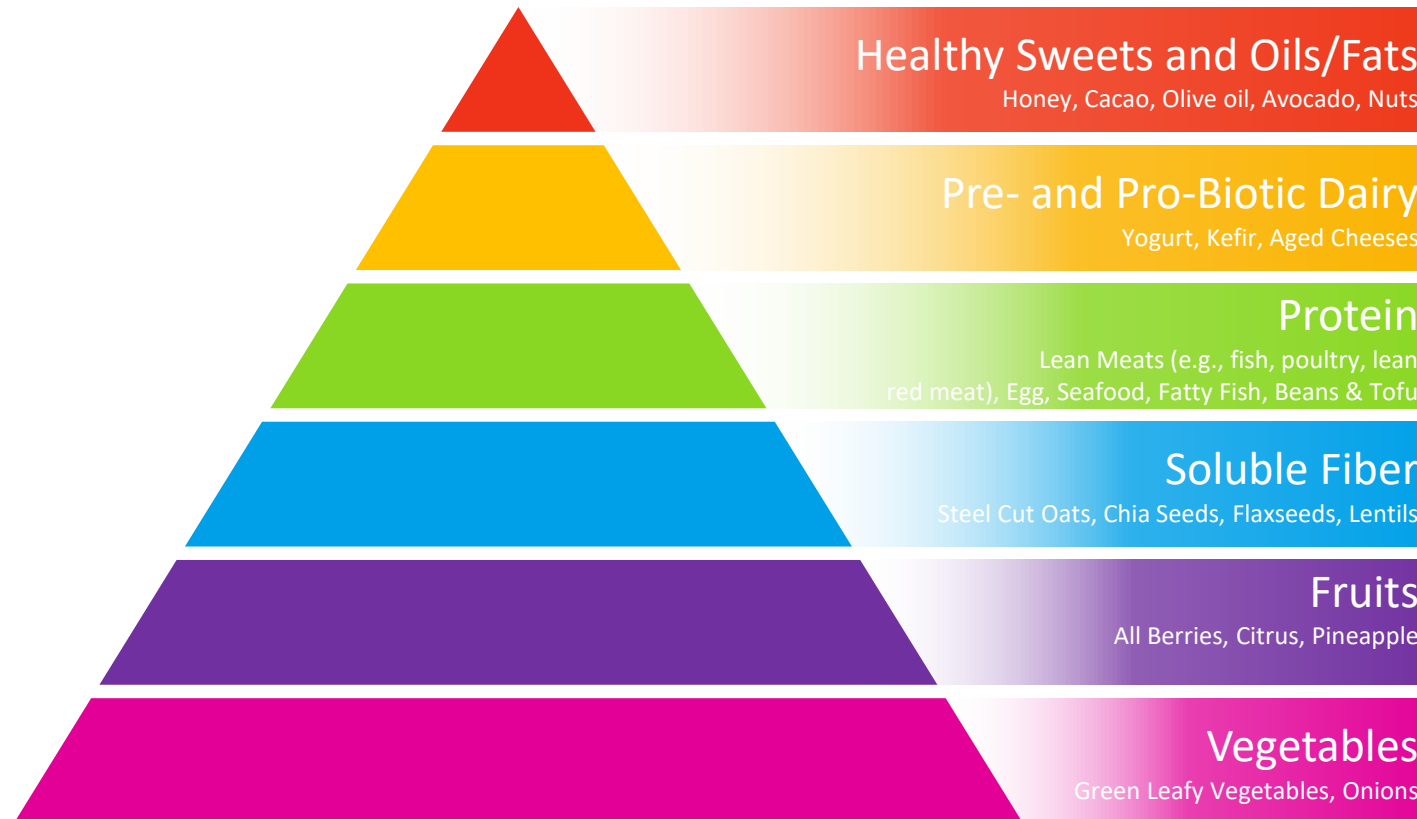
Mesa et al. *Cancer*. Jan 1 2007;109(1):68-76.

Mesa et al. *Blood*. November 16, 2008 2008;112(11):5224.

Mesa R A et al. *Blood*. 2007;110(11):2548

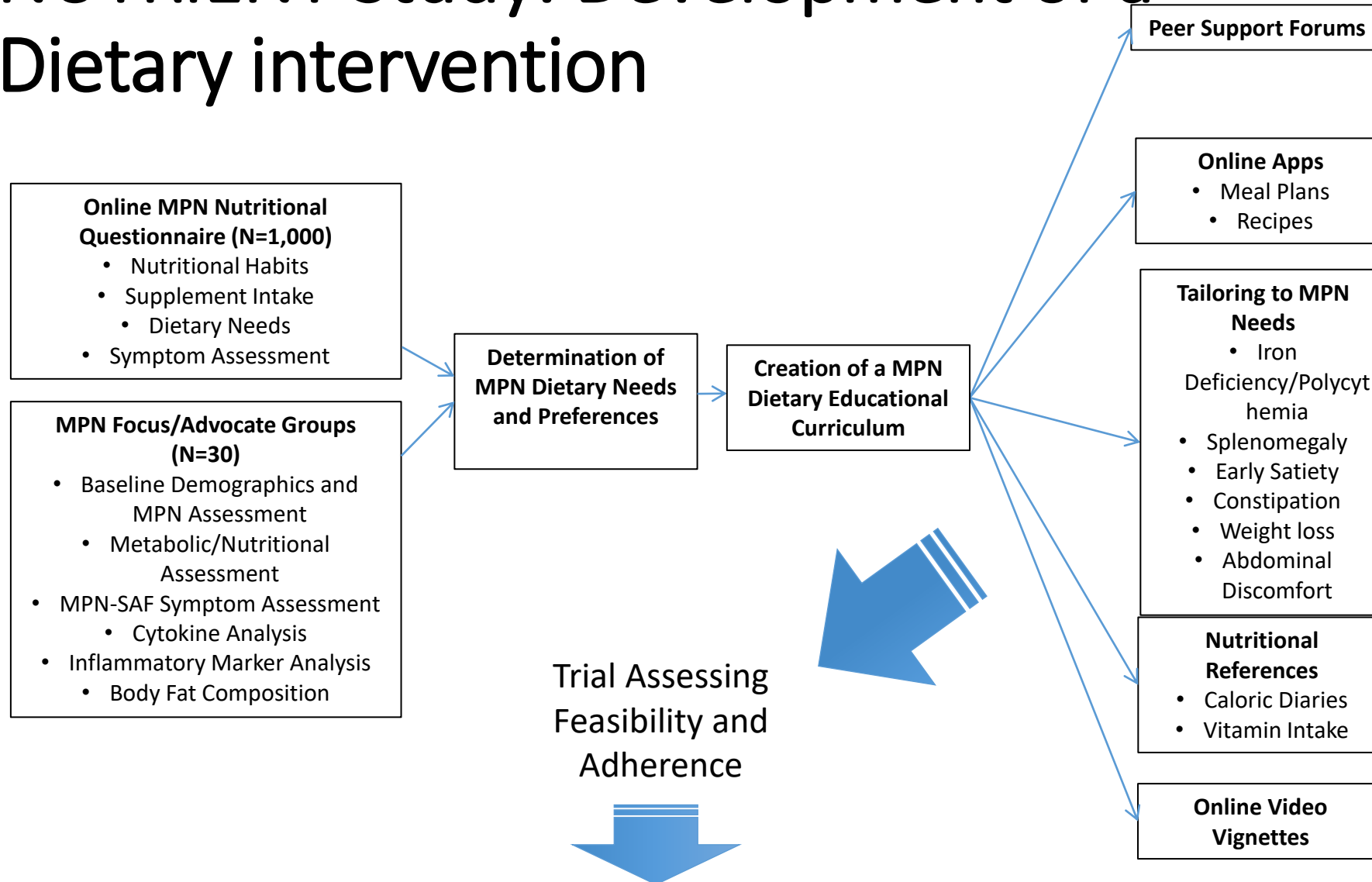
MPN Dietary Intervention Food Pyramid

Emphasizing Foods with Anti-inflammatory Properties

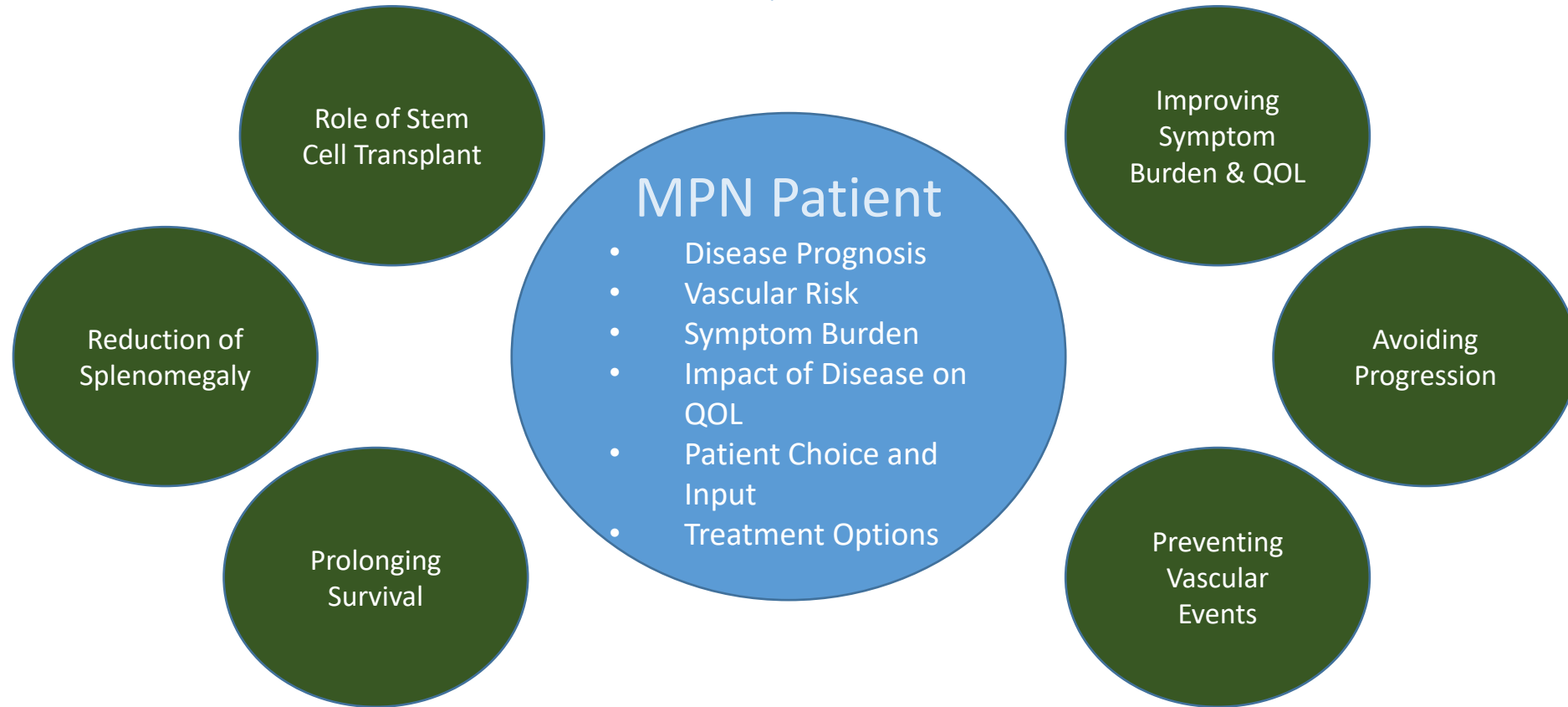


General Avoidance of: Processed Meats,
Refined Carbohydrates (e.g., soda pop),
Lard, Fried foods

NUTRIENT Study: Development of a Dietary intervention



Putting It All Together – MPNs and QOL



The Itch

I have an itch you cannot know,
not the least hint will ever show
No bump no rash no insect bite
provides a clue as to my plight
My clothes, a shower, the air I breathe
make my skin prickle and seethe
Constant reminders it provides
of the disease my body hides
Maddening tears the burning brings,
no scratch, no pills can stop the stings
Life is good,
it could be much worse
I can live with my itchy curse
I walk the dog to pass the time,
take deep breaths and clear my mind
Pruritus is a small price
for my wonderful blessed life

Paul Nudelman

Poet & PV Patient

Gurnee, IL, USA



Myeloproliferative Neoplasms

Multi-Disciplinary Team
Mayo Clinic, Arizona, USA

MPN Burden/
Symptom/QOL
Assessment

Improving
Transplant
Outcomes

New MPN
Drug/
Genetic
Therapies

Physical
Activity/
Behavioral
Therapies

