Guidelines and Gaps

MPNS 2019

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Director, UT Health San Antonio Cancer Center
Mays Family Foundation Distinguished University Presidential Chair

Twitter: @mpdrc

Mays Cancer Center
Welcome to Texas!
**Mays Cancer Center Catchment Area**

**Geography:**
- 38 counties
- 45,970 square miles
- Long distances from oncology care

- Population: 4.5 million
  - 69% Hispanic
  - 23% live in poverty
Our Mission: Decreasing the burden of cancer in San Antonio, South Texas and Beyond
Guidelines and Gaps 2019

MPNs

• Burden of having an MPN
• Treatment goals and “guidelines”
• What do we know?
• How do symptoms fit into our dealing with an MPN?
Assessing MPN Burden

WHO Diagnosis Does Not Tell Whole Story

**MPN Symptoms**
- MF > PV > ET
- Multifactorial
- Some ET/PV > MF
- Cytoreductive Rx frequently not effective

**Vascular Events**
- PV/ET > MF
- Counts matter
- Can be unrecognized

**Progression**
- PV/ET to MF
- PV/ET to AML
- MF to AML
- ? 2nd MDS

**Baseline Health**
Age/Medicines
Comorbidities

**Cytopenias**
- MF > ET/PV
- Anemia
  - MF 75%
  - TX Dep 25%
- TPN 30%

**Splenomegaly**
- MF > ET/PV
- Pain not always a function of size

**Cytoopenias**
- MF > ET/PV
- Anemia
  - MF 75%
  - TX Dep 25%
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**Baseline Health**
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- TPN 30%
Evolution of MPN Symptom Assessment Tools

- MF–SAF 2009 (19 items)
- MF-SAF 2.0 (7 items 2011)
- Blood 2011
- MF–SAF 2011 (27 items)
- MPN-SAF TSS (10 items 2012)
- JCO 2012

MPN-SAF Languages
- Albanian
- Czech
- Chinese
- Danish
- Dutch
- English
- French
- German
- Hebrew
- Hungarian
- Italian
- Japanese
- Portuguese
- Romanian
- Swedish
- Spanish
- Urdu
### English

**Know Your Score**

**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**

<table>
<thead>
<tr>
<th>Symptom Description</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td></td>
</tr>
<tr>
<td>Abdominal discomfort</td>
<td></td>
</tr>
<tr>
<td>Inactivity</td>
<td></td>
</tr>
<tr>
<td>Problems with concentration</td>
<td></td>
</tr>
<tr>
<td>Night sweats</td>
<td></td>
</tr>
<tr>
<td>Itching (pruritus)</td>
<td></td>
</tr>
<tr>
<td>Bone pain (stiffness, not joint pain or arthritis)</td>
<td></td>
</tr>
<tr>
<td>Fever (&gt; 37.5°C or 100°F)</td>
<td></td>
</tr>
<tr>
<td>Unintentional weight loss last 6 months</td>
<td></td>
</tr>
</tbody>
</table>

**Total:** ______________________

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.

You can also fill in this form and find more expert information about myeloproliferative neoplasms online at [www.spotlightonMPN.com](http://www.spotlightonMPN.com)

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### Arabic

**نموذج تقييم الأمراض**

**الاسم:** ______________________

**التاريخ:** ______________________

ملمع النظام التالي وانحرف الأمراض التي تشعر بها:

من الأعراض تقرب من 1 إلى 10، 0 إذا لم يشعر بها، و10 إذا ما شعر بذلك. 

أمراض في المظهر الآتي (الأعراض الإجمالية) من خلال توفير بعض الأعراض التي تشعر بها خلال مدة 24 ساعة:

<table>
<thead>
<tr>
<th>الأعراض</th>
<th>ملاحظة</th>
</tr>
</thead>
<tbody>
<tr>
<td>ضعف وقدر الهواء التي تمثل هذه</td>
<td>0</td>
</tr>
<tr>
<td>نقص في الوزن الذي تمثل هذه</td>
<td>0</td>
</tr>
</tbody>
</table>

إجمالي: ______________________

المراجع: [www.spotlightonMPN.com](http://www.spotlightonMPN.com)
MPN10: allows visual assessment

<table>
<thead>
<tr>
<th>Item</th>
<th>MPN-10 (Mayo Clinic)</th>
<th>MFSAF v2.0 (Incyte)</th>
<th>MFSAF-revised (Gilead)</th>
<th>MFSF v4.0 (Critical Path Institute)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>X</td>
<td></td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Night sweats</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Itching</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Abdominal discomfort</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Pain under ribs on left side</td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Early satiety</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Bone pain</td>
<td>X</td>
<td>X*</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Inactivity</td>
<td>X</td>
<td>X**</td>
<td>X**</td>
<td></td>
</tr>
<tr>
<td>Concentration problems</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fever</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight loss</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Scale score range</strong></td>
<td>0-100</td>
<td>0-60</td>
<td>0-70</td>
<td>0-70</td>
</tr>
</tbody>
</table>

* This item was “bone or muscle pain” for the MFSAF v2.0.
** This item was not used to compute the scale score.

Dueck et. al. 201
ASH 2018: myMPN Patient Registry

myMPN participation

myMPN

CHANGE YOUR PROGNOSIS

www.mympn.org

ASH 2018. Abstract ID: #119033
Employment change due to MPNs

Impact of Living with MPN Survey Trial: Yu et. al. ASH 2016
Classic Signs and Symptoms of MPNs

Geyer H L, and Mesa R A Blood 2014;124:3529-3537
MPN Pain Severity

Prospective online survey of 502 MPN patients (MF 26.9%, PV 44.2%, ET 28.9%)

Survey content included the Barriers Questionnaire II (BQII), MPN10

Chronic Pain Common Before MPNs
- Prevalence of chronic pain 47.1% prior to development of MPN
  - Chronic abdominal pain: 5.6%
  - Chronic bone/muscle pain: 20.8%

MPNs Drive Symptom Burden
- Mean MPN10 28.3
- MPNs induce moderate to severe symptom burden related to pain:
  - Abdominal pain severity (MPN10 3.1) and prevalence (65.6%)
  - Bone pain severity (MPN10 3.0) and prevalence (60.4%)

MPN Impacts Chronic Pain
- Since the MPN diagnosis, chronic pain either:
  - Stayed the same (26.2%)
  - Worsened (28.3%)
  - Significantly worsened (14.5%)

Pain is Treatable
- 42.1% of MPN patients regularly take medications to control pain
Treatments described as ‘Successful’ by MPN patients

<table>
<thead>
<tr>
<th></th>
<th>Abdominal Pain</th>
<th>Bone Pain</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Prior Treatments</td>
<td>Current Treatments</td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>61 (12.2%)</td>
<td>43 (8.6%)</td>
</tr>
<tr>
<td>Anti-inflammatory Agents</td>
<td>68 (13.5%)</td>
<td>48 (9.6%)</td>
</tr>
<tr>
<td>Short-Acting Opioids</td>
<td>50 (10.0%)</td>
<td>36 (7.2%)</td>
</tr>
<tr>
<td>Long-Acting Opioids</td>
<td>15 (3.0%)</td>
<td>14 (2.8%)</td>
</tr>
<tr>
<td>Gabapentin, Pregabalin</td>
<td>22 (4.4%)</td>
<td>11 (2.2%)</td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>10 (2.0%)</td>
<td>4 (0.8%)</td>
</tr>
<tr>
<td>Alcohol</td>
<td>14 (2.8%)</td>
<td>6 (1.2%)</td>
</tr>
<tr>
<td>Cannabis</td>
<td>31 (6.2%)</td>
<td>25 (5.0%)</td>
</tr>
<tr>
<td>Physical Therapy</td>
<td>17 (3.4%)</td>
<td>8 (1.6%)</td>
</tr>
<tr>
<td>Yoga</td>
<td>37 (7.4%)</td>
<td>27 (5.4%)</td>
</tr>
<tr>
<td>Daily Exercise</td>
<td>82 (16.3%)</td>
<td>81 (16.1%)</td>
</tr>
<tr>
<td>Tai Chi</td>
<td>8 (1.6%)</td>
<td>6 (1.2%)</td>
</tr>
<tr>
<td>Massage Therapy</td>
<td>38 (7.6%)</td>
<td>25 (5.0%)</td>
</tr>
<tr>
<td>Acupuncture</td>
<td>20 (4.0%)</td>
<td>7 (1.4%)</td>
</tr>
<tr>
<td>Biofeedback</td>
<td>4 (0.8%)</td>
<td>2 (0.4%)</td>
</tr>
<tr>
<td>Counseling</td>
<td>7 (1.4%)</td>
<td>6 (1.2%)</td>
</tr>
<tr>
<td>TENS</td>
<td>7 (1.4%)</td>
<td>6 (1.2%)</td>
</tr>
<tr>
<td>Meditation/Prayer</td>
<td>46 (9.2%)</td>
<td>40 (8.0%)</td>
</tr>
<tr>
<td>Trigger Point Injections</td>
<td>4 (0.8%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Chiropractor</td>
<td>31 (6.2%)</td>
<td>21 (4.2%)</td>
</tr>
</tbody>
</table>
Conclusions:

- Chronic non-MPN pain is further complicated by the development of the MPNs
- Many MPN patients lack understanding on MPN pain prevalence and furthermore feel ill-equipped to manage it
- Symptomatic benefit may be derived from various pharmacological and non-pharmacological treatment modalities
- MPN patients may benefit from early referral to Palliative Care or Pain Management
Guidelines and Gaps 2019

MPNs

• Burden of having an MPN
• Treatment goals and “guidelines”
• What do we know?
• How do symptoms fit into our dealing with an MPN?
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.

<table>
<thead>
<tr>
<th>Treatment Goal</th>
<th>Patients</th>
<th>Physicians</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptom improvement</td>
<td>18%</td>
<td>18%</td>
</tr>
<tr>
<td>Better quality of life</td>
<td>22%</td>
<td>24%</td>
</tr>
<tr>
<td>Slow/delay progression</td>
<td>20%</td>
<td>20%</td>
</tr>
<tr>
<td>Healthy blood counts</td>
<td>19%</td>
<td>19%</td>
</tr>
<tr>
<td>Reduction in spleen size</td>
<td>12%</td>
<td>12%</td>
</tr>
<tr>
<td>Prevention of ...</td>
<td>17%</td>
<td>17%</td>
</tr>
<tr>
<td>Reduce blood transfusions</td>
<td>14%</td>
<td>14%</td>
</tr>
<tr>
<td>Anaemia treatment</td>
<td>5%</td>
<td>6%</td>
</tr>
<tr>
<td>Haematocrit level less...</td>
<td>11%</td>
<td>11%</td>
</tr>
<tr>
<td>Reduce frequency of...</td>
<td>3%</td>
<td>3%</td>
</tr>
</tbody>
</table>

**What is your most important treatment goal for your condition?**

n: MF = 81, PV = 90, ET = 174

International MPN Landmark Study – Harrison et. al. ASH 2016
Treatment Goals

• Avoiding thrombosis and bleeding?
• Improving MPN associated symptoms?
• Increase activity?
• Decreasing splenomegaly?
• Improving anemia?
• Improving low platelets?
• Decreasing progression?
• Preventing progression?
• Live longer?
MPN Disease Course: When do problems occur?

- Diagnosis
- Counts
- Symptoms
- Progression
- Vascular
What is a treatment guideline?

Guideline – Guardrails

*The science of medicine*

How applied to an individual

*The art of medicine*
Management of ET 2019

1. Diagnosis of ET
2. Assess Survival & Disease Burden
3. Develop Treatment Plan
4. Front Line ET Medical Management
   - Progression to MF
   - Second Line & Beyond ET Medical Management
   - Progression to AML
Treatment Gaps - ET

1. What is the optimal front line therapy for ET?

2. How do we prevent disease progression?

3. What is the role of JAK inhibition?
Management of PV 2019

- Diagnosis of ET
- Assess Survival & Disease Burden
- Develop Treatment Plan

Front Line ET Medical Management

- Progression to MF
- Second Line & Beyond ET Medical Management
- Progression to AML
Treatment Gaps - PV

1. What is the optimal front line therapy for PV?

2. How do we prevent disease progression?

3. How early should we consider JAK inhibition?
Management of Myelofibrosis 2019

1. Diagnosis of Myelofibrosis (Primary/Post ET/Post PV)
2. Assess Survival & Disease Burden
3. Develop Treatment Plan
4. Front Line MF Medical Management
   - Stem Cell Transplant Soon
   - “Salvage” Transplant
   - Second Line MF Medical Management
   - AP/ Blast Phase Management
1. What is ruxolitinib failure and what should be the approach?

2. How can we further treat MF beyond JAKi and Allo Transplant?

3. How early should we consider JAK inhibition?
Guidelines and Gaps 2019

MPNs

- Burden of having an MPN
- Treatment goals and "guidelines"
- What do we know?
- How do symptoms fit into our dealing with an MPN?
**MPNs – Therapy Choices What We Know**

- Keeping the HCT <45% (at least) is important in PV, maybe in JAK2 mutated ET

- HU is front line choice in ET by good data, more tenuous front line choice in PV, and only supplemental role in MF

- INF is safe and effective in PV, less data in ET, may play role in some MF situations but less clear

- Anagrelide can be used in ET, but with toxicity plays a smaller role

- Ruxolitinib has a big impact in MF on spleen and symptoms and impact likely is deeper. Ruxo controls counts, spleen, symptoms and decreases thrombosis in PV. May play a backup role in ET

- Therapies for deeply blocking progression and/or therapy of accelerated or blast phase deeply needed
Guidelines and Gaps 2019

MPNs

• Burden of having an MPN
• Treatment goals and “guidelines”
• What do we know?
• How do symptoms fit into our dealing with an MPN?
### MPN Recent Phase III Trials

#### MPN Symptom Assessment

<table>
<thead>
<tr>
<th>Disease</th>
<th>Drug</th>
<th>MPN Symptom Tool</th>
</tr>
</thead>
<tbody>
<tr>
<td>MF</td>
<td>RUXO (COMFORT 1)</td>
<td>MF-SA 2.0</td>
</tr>
<tr>
<td>MF</td>
<td>RUXO (COMFORT 2)</td>
<td>FACT-LYM</td>
</tr>
<tr>
<td>MF</td>
<td>Fedratinib (JAKARTA)</td>
<td>MF-SA 2.0</td>
</tr>
<tr>
<td>MF</td>
<td>Pacritinib (PERSIST 1&amp;2)</td>
<td>MPN-SA 2.0</td>
</tr>
<tr>
<td>MF</td>
<td>Momelotinib (SIMLIFY 1&amp;2)</td>
<td>MPN-SA 2.0</td>
</tr>
<tr>
<td>MF</td>
<td>Pomalidomide (RESUME)</td>
<td>FACT-AN</td>
</tr>
<tr>
<td>MF</td>
<td>RUXO (RETHINK)</td>
<td>MPN-SA 2.0</td>
</tr>
<tr>
<td>PV</td>
<td>Ruxo (RESPONSE)</td>
<td>MPN-SA 2.0</td>
</tr>
<tr>
<td>PV</td>
<td>Ruxo (RELIEF)</td>
<td>MPN-SA 2.0</td>
</tr>
<tr>
<td>PV</td>
<td>PEG INFa2a (MPD-RC 112)</td>
<td>MPN-SA 2.0</td>
</tr>
<tr>
<td>ET</td>
<td>Ruxo (MAGIC)</td>
<td>MPN-SA 2.0</td>
</tr>
<tr>
<td>ET</td>
<td>PEG INFa2a (MPD-RC 112)</td>
<td>MPN-SA 2.0</td>
</tr>
</tbody>
</table>
Symptomatic Profiles of Patients With Polycythemia Vera: Implications of Inadequately Controlled Disease

Geyer et. al.
JCO 2015

N=1332 PV Patients
Pre JAK Inhibitors

Ongoing Phleb
HU Failure

Palpable Spleen

Mays Cancer Center
UT Health MD Anderson Cancer Center
Proportions of patient respondents who did not recognize common symptoms as being related to their myeloproliferative neoplasm.
Percentage of MPN patients who did not respond “none” when asked about symptoms at diagnosis.

Percentage of physicians who estimated that their patients had symptoms at diagnosis.

What do symptoms tell us about MPN Biology?

MPN Symptoms

Mood Disorders
Anxiety over Uncertainty

Cytokine Driven Symptoms
Spleen/Inflammation

Mays Cancer Center
UT Health San Antonio
MD Anderson Cancer Center
MPN “Fatigue” Project 2014
Collaborative Internet Based Trial with MPN Forum

Online 70 Item Survey
- Demographics
- MPN History
- MPN-SAIF (MPN10)
- Brief fatigue inventory (BFI)
- Profile of mood states (POMS-Short)
- Patient Health Questionnaire (PHQ-2)
- Mental Health Inventory (MHI-5)

Patients
- 1788 MPN patients/ 1676 Eval.
- ET 33%, PV 39%, MF 25%
- 68% Female, median age 59.
- MPN10 Score average 28.4 (range 0-83)

Psych Comorbidity
- 23% high likelihood of depression (≥ 3 on PHQ-2)
- Prior diagnosis depression (32%), anxiety (29%), stress (26%), grief (15%)
- 22% on therapy for mood disorder in last 6 months

MPN Correlation
- Higher BFI, MPN-SAIF, MPN10 scores all correlated with increased depressive symptoms (p<0.0001)

ANY MPN Patient
- Survey online
- MPN Forum
- MPN Advocacy
- MPN Research Foundation
- CMPD Ed Foundation

Register/ Online Consent

Scherber Cancer 2016
### Baseline, Patients with Myelofibrosis vs. Healthy Controls

<table>
<thead>
<tr>
<th></th>
<th>V617F−</th>
<th>V617F+</th>
</tr>
</thead>
<tbody>
<tr>
<td>PET</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCT</td>
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<tr>
<td>PET+</td>
<td></td>
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</tr>
<tr>
<td>PCT+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PMF+</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

S. Verstovsek, H. Kantarjian, R. Mesa, et. al. NEJM 2010;363:1117-27
Inflammatory Cytokines and Chemokines in the MPNs

Symptom Burden
- B2MG
- Ferritin
- VCAM1
- TNF-RII
- TIMP1
- PAL1
- IL-8
- Leptin
- IL-12
- TNF-1
- JAK2V617F
- INF
- IL15
- IL1B
- IL8
- INF
- INF
- IL12
- IL8
- IP10
- TNF-1
- Clonal expansion/blasts

Disease Advancement
- HGF
- Splenomegaly
- IL1RA
- BMP1
- BMP6
- BMP7
- BMP-Rcp2
- IL-12
- TNF-1
- Leptin
- PAL1
- TIMP1
- VCAM1

Inferior Survival
- INF
- IL1B
- IL17A
- IL17F
- IL8

The Sequelae of Inflammation in MPNs

- Inflammation
  - Fatigue
  - Weight loss
  - Fevers
  - Night sweats

- Thrombosis
  - Visceral Clots = Abdominal Pain
  - Pulmonary Clots = Cough
  - Cerebral Vein Thrombosis = Headache

- Bone Marrow Fibrosis
  - Bone Pain

- Extramedullary Hematopoiesis
  - Abdominal Pain
  - Early Satiety
  - Nausea
  - Constipation

- Splenomegaly

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Mays Cancer Center

UT Health San Antonio

MD Anderson Cancer Center
Why do MPNs Progress?

- **Clonal Progression** (accumulation of mutations?)
- **ET PV Early MF**
- **Microenvironment/Inflammation?**
- **Overt MF**
  - **Progressive Myelofibrosis**
  - **Death from Stable MF (Debilitation)**
  - **Acute Myeloid Leukemia**
What is Rux Failure in MF?

- Duration
- Spleen
- Progression
- Hemorrhage
- Thrombocytopenia
- Dose
- Transfusions
- Anemia
## The SIMM Survey: Integrative Medicine

### Intervention Comparisons for Symptom Burden, QOL, Depression, and Fatigue

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Overall N = 858</th>
<th>Aerobic Activity n=442</th>
<th>Massage n=244</th>
<th>Yoga n=220</th>
<th>Nutrition n=216</th>
<th>Strength training n=204</th>
<th>Acupuncture n=166</th>
<th>Meditation n=163</th>
<th>Breathing exercise n=158</th>
<th>Chiropractic n=139</th>
<th>Support groups n=124</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>MPN-SAF TSS mean</td>
<td>QoL mean</td>
<td>PHQ-2 odds ratio (95%CI)</td>
<td>BFI mean</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>yes / no</td>
<td>yes / no</td>
<td>(95%CI)</td>
<td></td>
<td>yes / no</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall N = 858</td>
<td>MPN-SAF TSS mean</td>
<td>QoL mean</td>
<td>PHQ-2 odds ratio (95%CI)</td>
<td>BFI mean</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Aerobic Activity n=442</td>
<td>33.2 / 39.7 **</td>
<td>4.2 / 5.2 **</td>
<td>0.60 (0.42, 0.86) **</td>
<td>5.1 / 5.9 **</td>
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<td>Massage n=244</td>
<td>40.5 / 35.3 **</td>
<td>5.0 / 4.6 *</td>
<td>1.05 (0.72, 1.55)</td>
<td>6.1 / 5.4 **</td>
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<tr>
<td>Yoga n=220</td>
<td>35.1 / 37.3</td>
<td>4.5 / 4.8</td>
<td>0.61 (0.39, 0.94) *</td>
<td>5.5 / 5.6</td>
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<td>Nutrition n=216</td>
<td>35.5 / 37.3</td>
<td>4.6 / 4.8</td>
<td>1.09 (0.71, 1.67)</td>
<td>5.5 / 5.6</td>
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<td>Strength training n=204</td>
<td>34.0 / 37.7 *</td>
<td>4.2 / 4.9 **</td>
<td>0.58 (0.37, 0.91) *</td>
<td>5.2 / 5.7 *</td>
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<tr>
<td>Acupuncture n=166</td>
<td>38.2 / 36.6</td>
<td>5.1 / 4.7</td>
<td>0.74 (0.47, 1.17)</td>
<td>5.9 / 5.5</td>
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<tr>
<td>Meditation n=163</td>
<td>35.4 / 37.3</td>
<td>4.7 / 4.8</td>
<td>0.62 (0.38, 1.01)</td>
<td>5.4 / 5.6</td>
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<tr>
<td>Breathing exercise n=158</td>
<td>39.5 / 36.4</td>
<td>5.1 / 4.7</td>
<td>1.47 (0.95, 2.28)</td>
<td>6.1 / 5.5</td>
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<td>Chiropractic n=139</td>
<td>36.7 / 37.0</td>
<td>4.8 / 4.8</td>
<td>0.75 (0.46, 1.21)</td>
<td>5.6 / 5.6</td>
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<td>Support groups n=124</td>
<td>42.3 / 36.0 **</td>
<td>5.4 / 4.6 **</td>
<td>1.45 (0.91, 2.31)</td>
<td>6.2 / 5.5 **</td>
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</table>

Results adjusted for alcohol consumption, smoking status, BMI, current dietary modification, and MPN

Gowin et. al. EHA 2017., article in preparation.
Non-Pharmacologic Approaches in the MPNs: Online-Streamed Yoga

MPN Patients Completing the Yoga Study (N=38)

Yoga participation averaged 50.8 min/week.

12 Week Online Yoga Course

Significant improvements in total symptom burden (effect size = -0.36, p=0.004)
- Anxiety (ES=-0.67, p=0.002)
- Depression (ES=-0.41, p=0.049)
- Sleep (ES=-0.58, p<0.001)
- Fatigue (ES=-0.33, p=0.04)

Patient Satisfaction:
- 68% of participants were either satisfied or very satisfied
- 75% felt that it was helpful for coping

Huberty et. al. Blood 2016 128:5478
MPN Yoga II - Pilot

Key Eligibility
- MPN Patient
- Not Depressed
- PS<3
- Not already doing yoga or Mindfullness
- <150 Min of weekly exercise

At Home Yoga (N=30)
- Active Yoga
  - 12 Weeks
  - >/= 60 Min/ Week
  - Fitbit tracking (Blinded)
  - Daily Logs-Yoga and activity
  - Blood (2 Timepoints)
    - TNFa
    - IL6
  - Saliva (2 Timepoints, 4x each timepoint)
    - Cortisol
  - MPN Sx, QOL, Sleep

Wait List Control (N=30)
- Wait List
  - 12 Weeks
  - Fitbit tracking/ Blinded
  - Usual Level of Activity
  - Daily Logs - Activity
  - MPN Sx, QOL, Sleep

MPN Yoga Team:
- Arizona State University: Jennifer Huberty PhD
- Linda Larkey, PhD
- Ryan Eckert, B.S.
- Mayo Clinic Arizona
- R. Mesa, MD
- Amylou Dueck, PhD
- K. Gowin, MD

Online Registration & Randomization

Post 12 week Cross Over
Major Findings

Patient-Reported Outcomes
   Significantly improved depression in the yoga group

Blood Draw Feasibility
   92.6% (n=25/27) completed the blood draw at baseline (week 0)
   70.4% (n=19/27) completed the blood draw at post-intervention (week 12)

Significant pre-post reduction in Tumor Necrosis Factor-Alpha (TNF-a) in the yoga group
   TNF-a is an inflammatory biomarker associated with worsened symptom burden in MPN patients

Huberty et. al. ASH 2017
Figure 3. Changes from Baseline in Patient-Reported Outcomes
4-Week *Calm* Meditation App Intervention in MPNs

**Study Purpose**

1. To examine the feasibility of delivering *Calm* meditation to MPN patients compared to a usual care control group.

2. To investigate the preliminary effects of *Calm* meditation on MPN patient-reported outcomes (fatigue, depression, anxiety, sleep disturbances, pain intensity, total symptom burden)

**Calm Meditation**
- 10 min/day of *Calm*
- Week 1 – “7 Days of *Calm***”
- Weeks 2-4 – “Daily *Calm***”

**Usual Care Control**
- Asked to maintain usual routine for 4 weeks
Results

Enrollment
112 enrolled
- 70 in Calm group
- 42 in control group

Meditation Participation (n=68 participated)
- 4-week Calm participation averaged ~72 min/week
- 42% achieved prescribed 10 min/day of meditation

Satisfaction (n=64 completed survey)
- 83% enjoyed/very much enjoyed the Calm app
- 97% would recommend the Calm app for other MPN patients
- 84% satisfied/very satisfied with the content of Calm

Effect Sizes
Small effects (0.2-0.5):
- Anxiety (d=-0.22)
- Depression (d=-0.29)
- Sleep disturbance (d=-0.47)
- Physical health (d=0.44)
- Fatigue (d=-0.27)
- Total symptom burden (d=-0.27)
Acceptance and Commitment Therapy for MPNs - The Opportunity

ACT in Chronic Conditions
- Chronic Pain
  - ↓ anxiety
  - ↓ pain
  - ↓ pain disability
  - ↑ QOL
- Fibromyalgia
  - ↑ mental QOL
- Chronic Fatigue
  - ↓ insomnia

ACT In Cancer
- Breast Cancer
  - Completed Cancer Treatment
  - ↓ Depressive
  - ↓ Anxiety
- CNS Tumors
  - Completed Cancer Treatment
  - ↑ QOL
  - ↑ QOL brain tumor specific

Padros, Geda, Stonnington & Mesa: Mayo Clinic
Non Pharmacological Approaches for MPN Burden Relief

- **Yoga**: Phase 2 trials ASH 2017
- **Physical Activity**: In development
- **Meditation**: Ongoing and Accrued
- **Nutrition**: Scherber ASH 2017
- **Diet Intervention**: In Preparation
- **ACT Therapy**: Ongoing