

Supplemental Table 1: Description of Study Questionnaires

Instrument	Description	Scoring	Metric
Quality of Life in Myelodysplasia Scale (QUALMS)	38-item MDS-specific questionnaire <ul style="list-style-type: none"> 3 subscales: Physical Burden, Emotional Burden, and Benefit Finding 	Mean score derived from 5-point Likert-type item-scores ranging from: <ul style="list-style-type: none"> 0 (always) to 5 (never) 	QUALMS Mean Score Range: 0-100 Higher scores indicate better QOL
5-level EQ-5D (EQ-5D-5L)	5-item health questionnaire <ul style="list-style-type: none"> Describes health based on mobility, self-care, usual activities, pain, anxiety Single value index for self-rating of overall health status used 	Single value index on 100-point overall scale ranging from: <ul style="list-style-type: none"> 0 (worse health imaginable) to 100 (best health imaginable) 	EQ-5D-5L Single Index Range: 0-100 Higher scores indicate better QOL
Patient Reported Outcomes Measurement Information System (PROMIS) Fatigue Short Form 7a	7-item instrument <ul style="list-style-type: none"> Assesses frequency of fatigue symptoms for ranges of chronic diseases 	T-Score derived from sum of 5-point Likert-type item-scores ranging from: <ul style="list-style-type: none"> 1 (never) to 5 (always) 	PROMIS Fatigue T-Score Range: 29.4-83.2 Higher scores indicate worse QOL
Functional Assessment of Cancer Therapy – General (FACT-G)	27-item instrument <ul style="list-style-type: none"> Includes physical, functional, social, and emotional well-being subscales 	Total score derived from sum of 5-point Likert-type item-scores ranging from: <ul style="list-style-type: none"> 0 (very much) to 4 (not at all) 	FACT-G Total Score Range: 0-108 Higher scores indicate better QOL
Vulnerable Elders Survey (VES-13)	13-item questionnaire <ul style="list-style-type: none"> Designed for screening participants at risk for health deterioration Includes domains of age, self-rated health, and limitations in physical function and disability 	Overall scale derived from domain-specific subscales: <u>Age (1-item):</u> <ul style="list-style-type: none"> 0 (<75) to 3 (≥85) <u>Self-rated health (1-item):</u> <ul style="list-style-type: none"> 0 (Excellent) to 1 (Poor or Fair) <u>Difficulty with Physical Activities (6-items):</u> <ul style="list-style-type: none"> 0 (no difficulty) to 1 (unable to perform) Maximum domain score of 2 <u>Difficulty with Activities that Require Assistance (5-items):</u> <ul style="list-style-type: none"> 0 (no difficulty) to 1 (difficulty or unable to perform) Domain score of 0 or 4 	VES-13 Total Score* Range: 0-10 Higher scores indicate worse QOL *VES ≥ 3 considered Frail (Vulnerable)

Supplemental Table 2: Summary of Baseline Characteristics by Vulnerability Subgroup, MDS only

Characteristic	Statistic	Vulnerable ¹ (N=83)	Not Vulnerable (N=165)	All (N=248)	P-value
Age	Mean ± SD	76.6 ± 9.9	69.4 ± 9.3	71.8 ± 10.1	< 0.001
Gender	Female, n(%)	31 (37%)	55 (33%)	86 (35%)	0.57
	Male, n(%)	52 (63%)	110 (67%)	162 (65%)	
Race	American Indian/Alaska Native, n(%)	2 (2%)	0 (0%)	2 (1%)	0.06
	Asian, n(%)	1 (1%)	0 (0%)	1 (0%)	
	Black, n(%)	2 (2%)	3 (2%)	5 (2%)	
	Native Hawaiian/Pacific Islander, n(%)	0 (0%)	0 (0%)	0 (0%)	
	White, n(%)	75 (90%)	160 (97%)	235 (95%)	
	More Than One Race, n(%)	0 (0%)	0 (0%)	0 (0%)	
	Unknown/Not Reported, n(%)	3 (3%)	2 (1%)	5 (2%)	
Ethnicity	Hispanic or Latino, n(%)	3 (4%)	1 (1%)	4 (2%)	0.22
	Not Hispanic or Latino, n(%)	78 (94%)	159 (96%)	237 (96%)	
	Unknown/Not Reported, n(%)	2 (2%)	5 (3%)	7 (3%)	
BMI	Mean ± SD	29.9 ± 8.7	28.7 ± 4.8	29.1 ± 6.3	0.17
Blast %	Mean ± SD	3.6 ± 3.6	4.3 ± 5.2	4.1 ± 4.7	0.27
Hemoglobin (g/dL)	<8, n(%)	17 (20%)	25 (15%)	42 (17%)	0.02
	8-10, n(%)	37 (45%)	53 (32%)	90 (36%)	
	>10, n(%)	29 (35%)	87 (53%)	116 (47%)	
Platelets (10 ⁹ /L)	<50, n(%)	0 (0%)	0 (0%)	0 (0%)	-
	≥50, n(%)	83 (100%)	165 (100%)	248 (100%)	
ANC (10 ⁶ /L)	<800, n(%)	8 (10%)	36 (22%)	44 (18%)	0.03
	≥800, n(%)	71 (86%)	127 (80%)	198 (80%)	
	Missing, n(%)	4 (4%)	2 (1%)	6 (2%)	
IPSS-R	Very Low, n(%)	15 (18%)	41 (25%)	56 (23%)	0.23
	Low, n(%)	26 (31%)	46 (28%)	72 (29%)	
	Intermediate, n(%)	11 (13%)	35 (21%)	46 (19%)	
	High, n(%)	13 (16%)	15 (9%)	28 (11%)	
	Very High, n(%)	10 (12%)	19 (12%)	29 (12%)	
	Not Calculated, n(%)	8 (10%)	9 (5%)	17 (7%)	

N = Number of participants in each category. Fisher's exact test used for comparing proportions of demographic factors between disease groups. An analysis of variance (ANOVA) used for comparing means of demographic factors between disease groups. SD = Standard Deviation. BMI=Body Mass Index. IPSS-R=International Prognostic Scoring System. ¹Vulnerable participants are those with VES-13 ≥3.

Supplemental Table 3: Summary of Baseline HRQoL Scores by Disease Subgroup and Vulnerability Subgroup

QOL Measure	Statistic	MDS (N=248)		MDS/MPN (N=40)		ICUS (N=48)		AML<30% (N=15)		At-Risk (N=98)	
		Vulnerable (N=84)	Not Vulnerable (N=164)	Vulnerable (N=18)	Not Vulnerable (N=22)	Vulnerable (N=12)	Not Vulnerable (N=36)	Vulnerable (N=5)	Not Vulnerable (N=10)	Vulnerable (N=30)	Not Vulnerable (N=68)
QUALMS Mean Score	Mean (95% CI)	63.1 (60.3, 66.0)	73.2 (71.1, 75.2)	66.5 (60.4, 72.6)	75.0 (69.4, 80.6)	64.9 (57.5, 72.3)	76.8 (72.5, 81.2)	52.5 (41.0, 64.0)	72.6 (64.1, 81.2)	67.5 (62.7, 72.2)	75.9 (72.7, 79.2)
	P-value	<0.001	-	0.045	-	0.013	-	0.013	-	0.013	-
QUALMS Physical Burden	Mean (95% CI)	56.5 (52.9, 60.0)	72.7 (70.2, 75.3)	58.4 (50.8, 66.0)	77.3 (70.3, 84.2)	61.4 (52.2, 70.6)	72.3 (66.9, 77.7)	45.3 (31.1, 59.6)	79.1 (68.4, 89.7)	64.0 (58.2, 69.9)	75.8 (71.8, 79.8)
	P-value	<0.001	-	0.001	-	0.045	-	<0.001	-	0.003	-
QUALMS Benefit Finding	Mean (95% CI)	58.4 (52.9, 63.9)	59.5 (55.5, 63.5)	58.0 (46.2, 69.8)	55.1 (44.3, 66.0)	58.3 (44.0, 72.6)	59.3 (50.9, 67.7)	56.6 (34.4, 78.8)	54.6 (38.1, 71.1)	53.4 (44.3, 62.5)	54.3 (48.1, 60.5)
	P-value	0.909	-	0.909	-	0.909	-	0.909	-	0.909	-
QUALMS Emotional	Mean (95% CI)	67.7 (63.7, 71.8)	72.8 (69.9, 75.7)	72.1 (63.4, 80.7)	73.1 (65.2, 81.0)	64.6 (54.2, 75.1)	82.8 (76.7, 89.0)	58.9 (42.6, 75.1)	66.0 (53.9, 78.1)	71.5 (64.8, 78.1)	77.1 (72.6, 81.7)
	P-value	0.202	-	0.869	-	0.017	-	0.869	-	0.518	-
FACT-G Total Score	Mean (95% CI)	73.8 (70.5, 77.1)	85.1 (82.7, 87.5)	75.5 (68.3, 82.8)	85.6 (79.3, 91.9)	73.7 (64.3, 83.0)	88.1 (83.1, 93.2)	64.7 (51.5, 78.0)	91.3 (81.9, 100.6)	74.3 (68.7, 79.8)	86.1 (82.4, 89.9)
	P-value	<0.001	-	0.040	-	0.015	-	0.004	-	0.002	-
FACT-G Physical Well-Being	Mean (95% CI)	19.6 (18.6, 20.6)	23.9 (23.2, 24.6)	19.4 (17.4, 21.5)	25.0 (23.2, 26.9)	20.2 (17.7, 22.7)	23.7 (22.3, 25.2)	16.5 (12.6, 20.4)	25.3 (22.6, 28.1)	20.9 (19.2, 22.5)	24.2 (23.2, 25.3)
	P-value	<0.001	-	<0.001	-	0.018	-	<0.001	-	0.002	-
FACT-G Social Well-Being	Mean (95% CI)	22.2 (20.9, 23.4)	22.7 (21.8, 23.6)	22.7 (20.0, 25.3)	22.1 (19.7, 24.5)	18.6 (15.4, 21.9)	23.7 (21.8, 25.6)	22.4 (17.3, 27.4)	24.1 (20.6, 27.7)	19.7 (17.6, 21.8)	22.8 (21.4, 24.2)
	P-value	0.763	-	0.763	-	0.042	-	0.763	-	0.063	-
FACT-G Emotional Well-Being	Mean (95% CI)	17.3 (16.3, 18.2)	18.6 (17.9, 19.2)	17.9 (15.9, 19.9)	17.0 (15.3, 18.8)	16.6 (14.2, 19.0)	19.5 (18.0, 20.9)	12.8 (9.0, 16.5)	19.8 (17.2, 22.4)	17.1 (15.6, 18.7)	19.0 (17.9, 20.0)
	P-value	0.104	-	0.525	-	0.104	-	0.012	-	0.104	-
FACT-G Functional Well-Being	Mean (95% CI)	15.0 (13.7, 16.4)	20.0 (19.1, 21.0)	15.3 (12.4, 18.1)	21.3 (18.8, 23.9)	15.9 (12.5, 19.3)	21.9 (19.9, 23.9)	12.8 (7.5, 18.1)	22.1 (18.3, 25.8)	16.3 (14.1, 18.6)	21.0 (19.5, 22.4)
	P-value	<0.001	-	0.006	-	0.006	-	0.006	-	0.003	-
EQ-5D-5L Total Score	Mean (95% CI)	59.9 (55.9, 63.8)	75.8 (73.0, 78.6)	67.0 (58.5, 75.4)	78.6 (71.0, 86.1)	61.3 (51.0, 71.5)	79.5 (73.4, 85.5)	40.9 (25.0, 56.7)	75.8 (64.6, 87.0)	65.2 (58.6, 71.9)	77.0 (72.7, 81.4)
	P-value	<0.001	-	0.044	-	0.008	-	0.002	-	0.008	-
PROMIS Fatigue Mean T-Score	Mean (95% CI)	56.0 (54.3, 57.6)	49.5 (48.3, 50.7)	52.7 (49.1, 56.3)	48.4 (45.2, 51.6)	55.1 (50.8, 59.5)	50.4 (47.9, 52.9)	57.1 (50.3, 63.8)	46.6 (41.9, 51.4)	53.5 (50.6, 56.3)	50.1 (48.2, 51.9)
	P-value	<0.001	-	0.079	-	0.079	-	0.054	-	0.079	-

N = Number of participants in each disease group with an observed QOL score and vulnerability data. Estimates based on ANCOVA model adjusted for age. P-values for pairwise comparisons adjusted using the Hochberg procedure. Vulnerable defined as VES-13 \geq 3. HRQoL=Health-related quality of life. QUALMS=Quality of Life in Myelodysplasia Scale. EQ-5D-5L=5-level EQ-5D-5L. FACT-G=Functional Assessment of Cancer Therapy – General; Patient Reported Outcomes Measurement Information System=PROMIS Short-Form Fatigue; VES-13=13-item Vulnerable Elders Survey.

Supplemental Table 4: Summary of Baseline HRQoL Scores by IPSS-R Score in MDS or MDS/MPN Overlap

		MDS or MDS/MPN Overlap by Collapsed IPSS-R Scores		
QOL Measure	Statistic	Very Low or Low (N=149)	Intermediate (N=54)	High or Very High (N=58)
QUALMS Mean Score	Mean (95% CI)	71.2 (69.0, 73.5)	70.4 (66.7, 74.0)	66.8 (63.2, 70.3)
	P-value	0.046	-	-
QUALMS Physical Burden	Mean (95% CI)	69.2 (66.3, 72.1)	68.8 (64.0, 73.5)	62.3 (57.7, 66.9)
	P-value	0.020	-	-
QUALMS Benefit Finding	Mean (95% CI)	61.5 (57.6, 65.5)	58.8 (52.3, 65.4)	53.5 (47.1, 59.9)
	P-value	0.039	-	-
QUALMS Emotional	Mean (95% CI)	71.0 (67.9, 74.2)	70.5 (65.4, 75.6)	71.4 (66.4, 76.3)
	P-value	0.941	-	-
FACT-G Total Score	Mean (95% CI)	82.4 (79.7, 85.1)	82.1 (77.5, 86.6)	79.3 (75.0, 83.6)
	P-value	0.265	-	-
FACT-G Physical Well-Being	Mean (95% CI)	22.7 (21.9, 23.6)	23.1 (21.8, 24.5)	21.4 (20.1, 22.7)
	P-value	0.149	-	-
FACT-G Social Well-Being	Mean (95% CI)	22.7 (21.8, 23.7)	22.3 (20.7, 23.9)	22.3 (20.8, 23.9)
	P-value	0.628	-	-
FACT-G Emotional Well-Being	Mean (95% CI)	18.0 (17.3, 18.7)	18.5 (17.4, 19.6)	18.2 (17.1, 19.3)
	P-value	0.685	-	-
FACT-G Functional Well-Being	Mean (95% CI)	18.8 (17.8, 19.9)	18.5 (16.7, 20.3)	17.4 (15.7, 19.1)
	P-value	0.185	-	-
EQ-5D-5L Total Score	Mean (95% CI)	73.4 (70.2, 76.5)	72.7 (67.5, 77.8)	64.1 (59.1, 69.1)
	P-value	0.005	-	-
PROMIS Fatigue Mean T-Score	Mean (95% CI)	50.9 (49.6, 52.3)	50.7 (48.5, 53.0)	53.3 (51.2, 55.5)
	P-value	0.100	-	-

N = Number of participants in each disease group with an observed IPSS-R score. Estimates based on ANCOVA model adjusted for age. Estimates and p-value based on linear regression of QOL score and IPSS-R score adjusted for age. HRQoL=Health-related quality of life. QUALMS=Quality of Life in Myelodysplasia Scale. EQ-5D-5L=5-level EQ-5D-5L. FACT-G=Functional Assessment of Cancer Therapy – General; Patient Reported Outcomes Measurement Information System=PROMIS Short-Form Fatigue; VES-13=13-item Vulnerable Elders Survey.

Supplemental Table 5: Summary of Baseline HRQoL Scores by IPSS-R Score and Vulnerability Subgroups in MDS or MDS/MPN Overlap

MDS and MDS/MPN Overlap by Collapsed IPSS-R Scores and Vulnerability Subgroup							
QOL Measure	Statistic	Vulnerable (N=89)			Not Vulnerable (N=172)		
		Very Low or Low (N=49)	Intermediate (N=16)	High or Very High (N=24)	Very Low or Low (N=100)	Intermediate (N=38)	High or Very High (N=34)
QUALMS Mean Score	Mean (95% CI)	63.6 (59.7, 67.4)	63.6 (57.3, 70.0)	62.7 (57.6, 67.9)	74.7 (72.1, 77.3)	73.6 (69.4, 77.7)	70.4 (66.0, 74.8)
	P-value	0.639			0.083		
QUALMS Physical Burden	Mean (95% CI)	55.8 (51.0, 60.6)	60.7 (52.8, 68.6)	54.9 (48.4, 61.3)	75.4 (72.2, 78.6)	72.8 (67.6, 77.9)	68.9 (63.4, 74.4)
	P-value	0.394			0.020		
QUALMS Benefit Finding	Mean (95% CI)	63.7 (56.4, 71.0)	57.9 (46.0, 69.8)	52.1 (42.4, 61.8)	60.5 (55.6, 65.4)	59.2 (51.3, 67.1)	54.4 (45.9, 63.0)
	P-value	0.030			0.287		
QUALMS Emotional	Mean (95% CI)	67.4 (61.7, 73.1)	62.6 (53.3, 71.9)	71.3 (63.7, 78.9)	72.7 (68.8, 76.5)	74.0 (67.9, 80.1)	71.8 (65.3, 78.3)
	P-value	0.406			0.881		
FACT-G Total Score	Mean (95% CI)	71.5 (66.8, 76.3)	77.5 (69.8, 85.1)	74.7 (68.5, 80.9)	87.2 (84.0, 90.3)	84.6 (79.4, 89.8)	83.6 (78.3, 88.9)
	P-value	0.113			0.118		
FACT-G Physical Well-Being	Mean (95% CI)	18.5 (17.1, 19.8)	21.6 (19.3, 23.8)	19.3 (17.5, 21.2)	24.6 (23.7, 25.5)	24.0 (22.5, 25.5)	23.3 (21.7, 24.8)
	P-value	0.106			0.038		
FACT-G Social Well-Being	Mean (95% CI)	22.3 (20.5, 24.1)	22.7 (19.7, 25.6)	22.2 (19.8, 24.6)	23.0 (21.8, 24.2)	22.2 (20.2, 24.1)	22.5 (20.4, 24.5)
	P-value	0.895			0.562		
FACT-G Emotional Well-Being	Mean (95% CI)	16.6 (15.4, 17.8)	17.5 (15.5, 19.6)	18.6 (16.9, 20.2)	18.6 (17.8, 19.5)	19.0 (17.6, 20.4)	18.0 (16.6, 19.5)
	P-value	0.036			0.457		
FACT-G Functional Well-Being	Mean (95% CI)	14.4 (12.6, 16.3)	15.7 (12.7, 18.7)	14.6 (12.2, 17.0)	20.8 (19.6, 22.0)	20.0 (18.0, 21.9)	19.9 (17.8, 22.0)
	P-value	0.290			0.260		
EQ-5D-5L Total Score	Mean (95% CI)	63.3 (57.8, 68.7)	64.0 (55.0, 73.0)	57.2 (49.9, 64.5)	77.9 (74.2, 81.5)	76.8 (70.9, 82.7)	70.1 (63.8, 76.4)
	P-value	0.899			0.014		
PROMIS Fatigue Mean T-Score	Mean (95% CI)	56.1 (53.8, 58.4)	53.8 (50.0, 57.6)	56.7 (53.5, 59.8)	48.7 (47.1, 50.2)	49.2 (46.7, 51.7)	50.4 (47.8, 53.1)
	P-value	0.667			0.175		

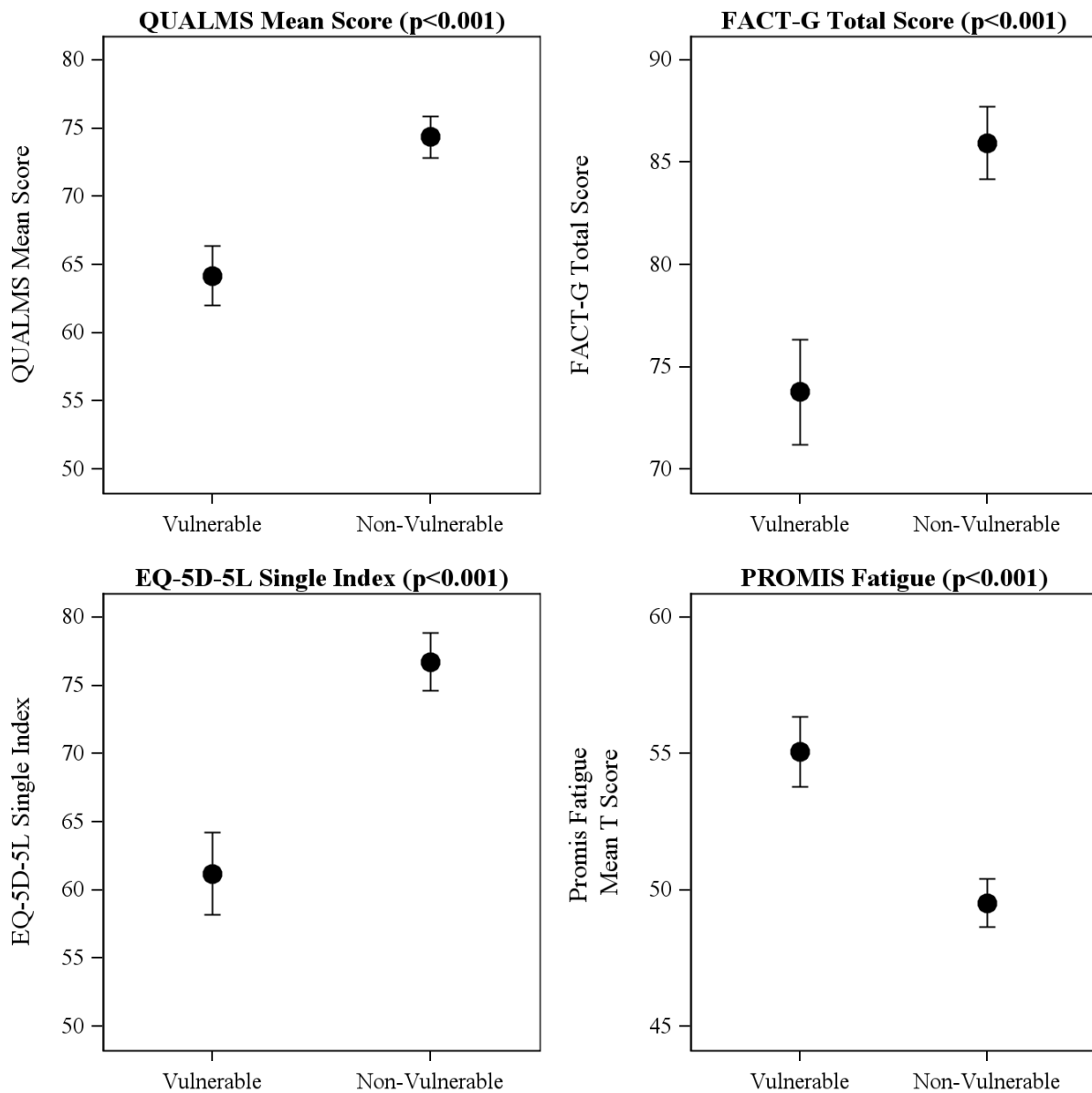
P-values for trend tests based on separate linear regression models by vulnerability subgroup all adjusted for age.

N = Number of participants in each category with observed IPSS-R. HRQoL=Health-related quality of life.

QUALMS=Quality of Life in Myelodysplasia Scale. EQ-5D-5L=5-level EQ-5D-5L. FACT-G=Functional Assessment of Cancer Therapy – General; Patient Reported Outcomes Measurement Information System=PROMIS Short-Form

Fatigue; VES-13=13-item Vulnerable Elders Survey.

Supplemental Figure 1: Summary of HRQoL Scores by Vulnerability Subgroup Among all Disease Subgroups

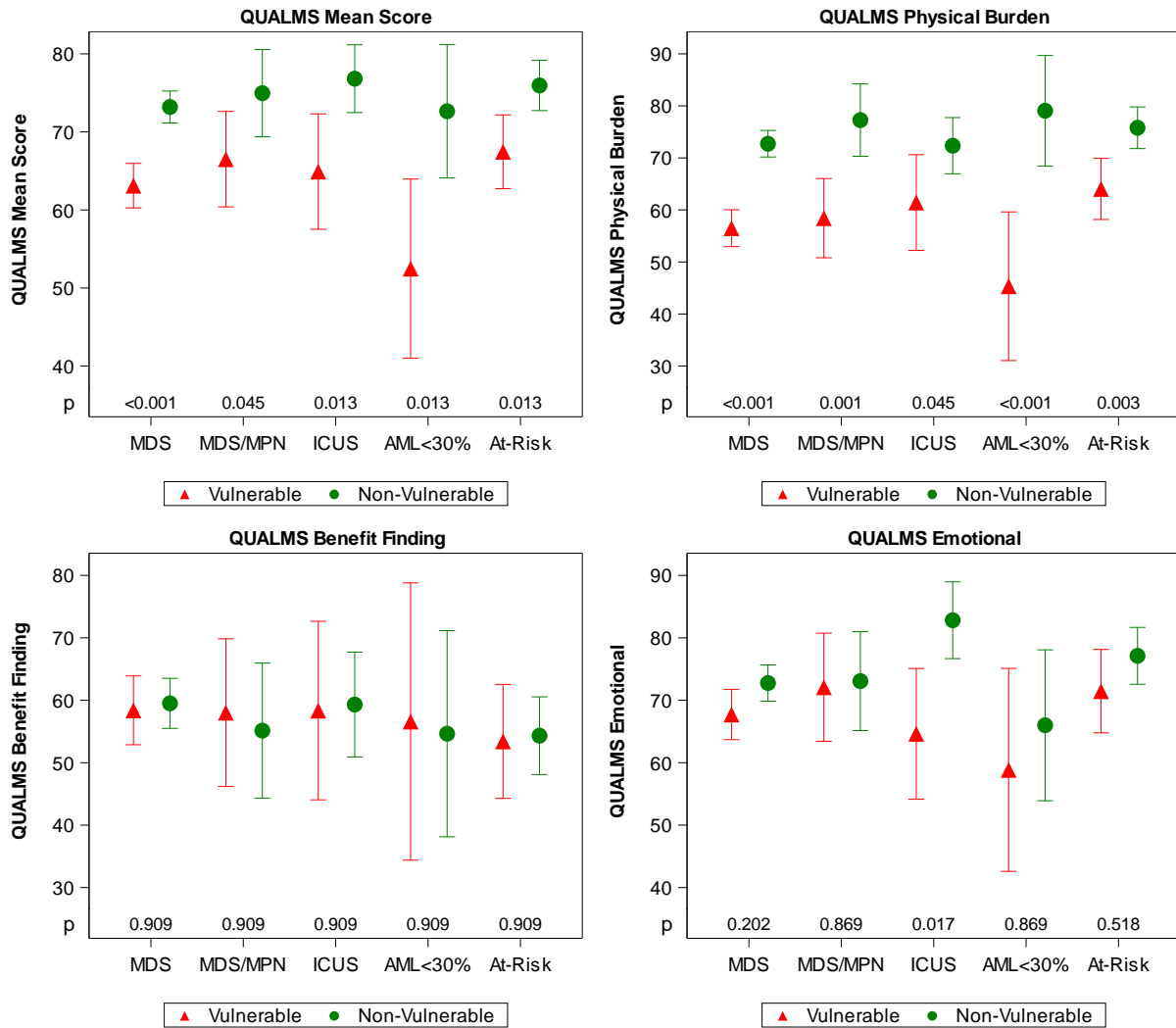


Number of participants (N) in each vulnerability subgroup pooled over all disease subgroups: Vulnerable (N=149), Non-Vulnerable (N=300).

Estimates and p-values based on ANCOVA model adjusted for age. HRQoL=Health-related quality of life.

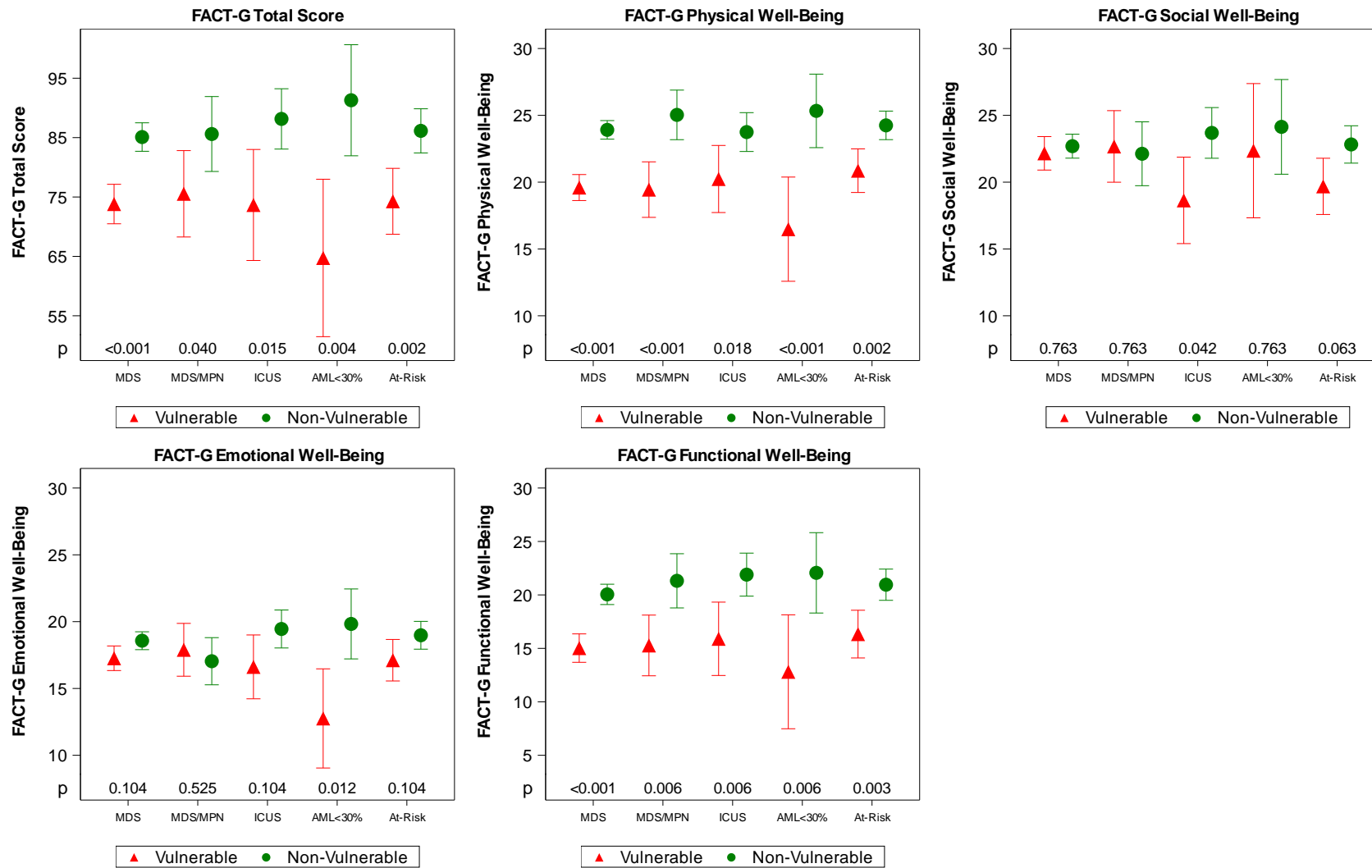
QUALMS=Quality of Life in Myelodysplasia Scale. EQ-5D-5L=5-level EQ-5D-5L. FACT-G=Functional Assessment of Cancer Therapy – General; Patient Reported Outcomes Measurement Information System=PROMIS Short-Form Fatigue; VES-13=13-item Vulnerable Elders Survey.

Supplemental Figure 2: Summary of QUALMS Scores by Vulnerability Subgroup Among and Disease Subgroup



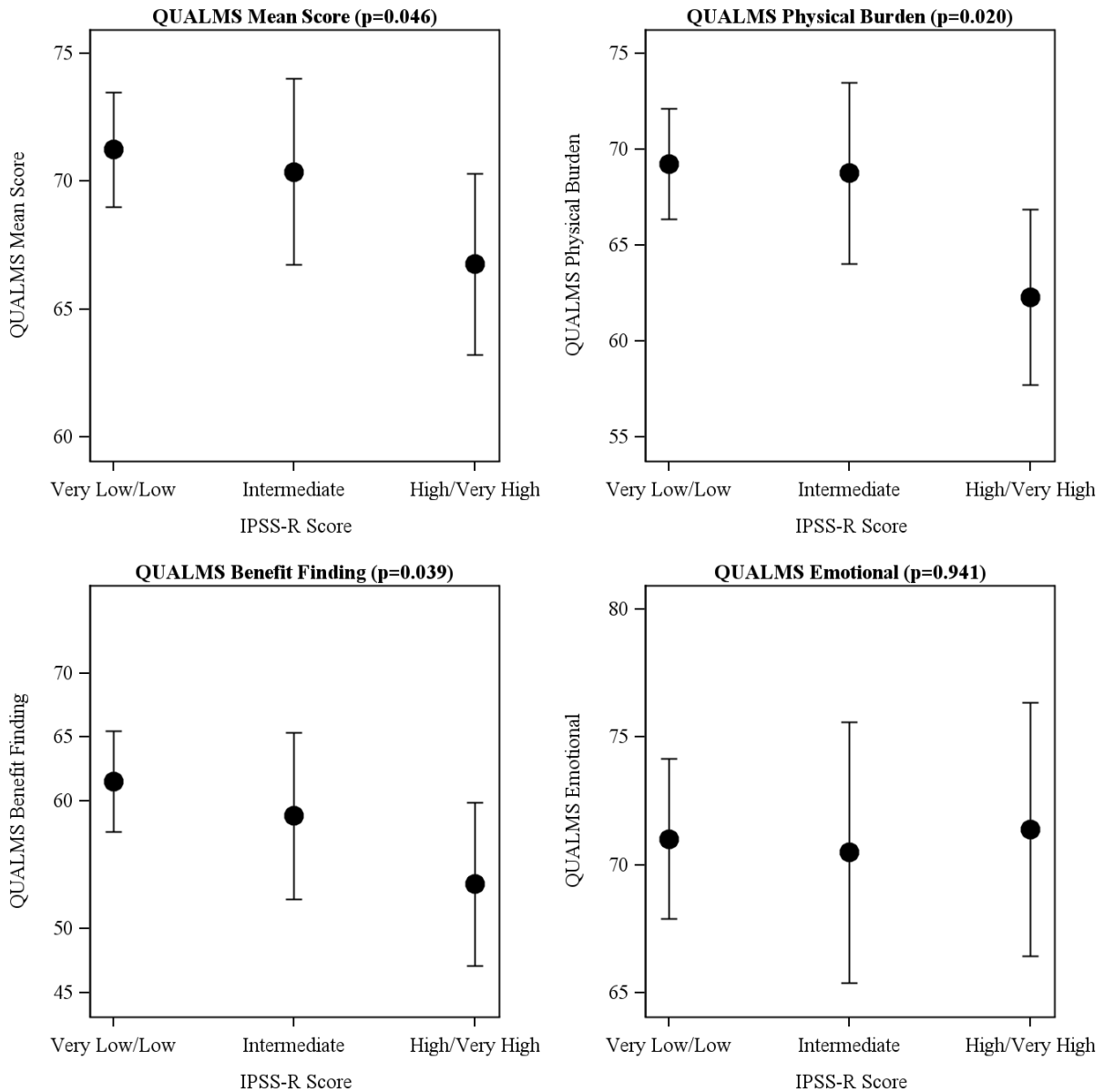
Number of participants (N) in each disease and vulnerability: Vulnerable MDS (N=84), MDS/MPN (N=18), ICUS (N=12), AML<30% (N=5), At-Risk (N=30), Non-Vulnerable MDS (N=164), MDS/MPN (N=22), ICUS (N=36), AML<30% (N=10), At-Risk (N=68). Estimates based on ANCOVA model adjusted for age. P-values for pairwise comparisons adjusted using the Hochberg procedure. Vulnerable defined as VES-13 \geq 3. HRQoL=Health-related quality of life. QUALMS=Quality of Life in Myelodysplasia Scale. VES-13=13-item Vulnerable Elders Survey.

Supplemental Figure 3: Summary of FACT-G Scores by Vulnerability Subgroup Among and Disease Subgroup



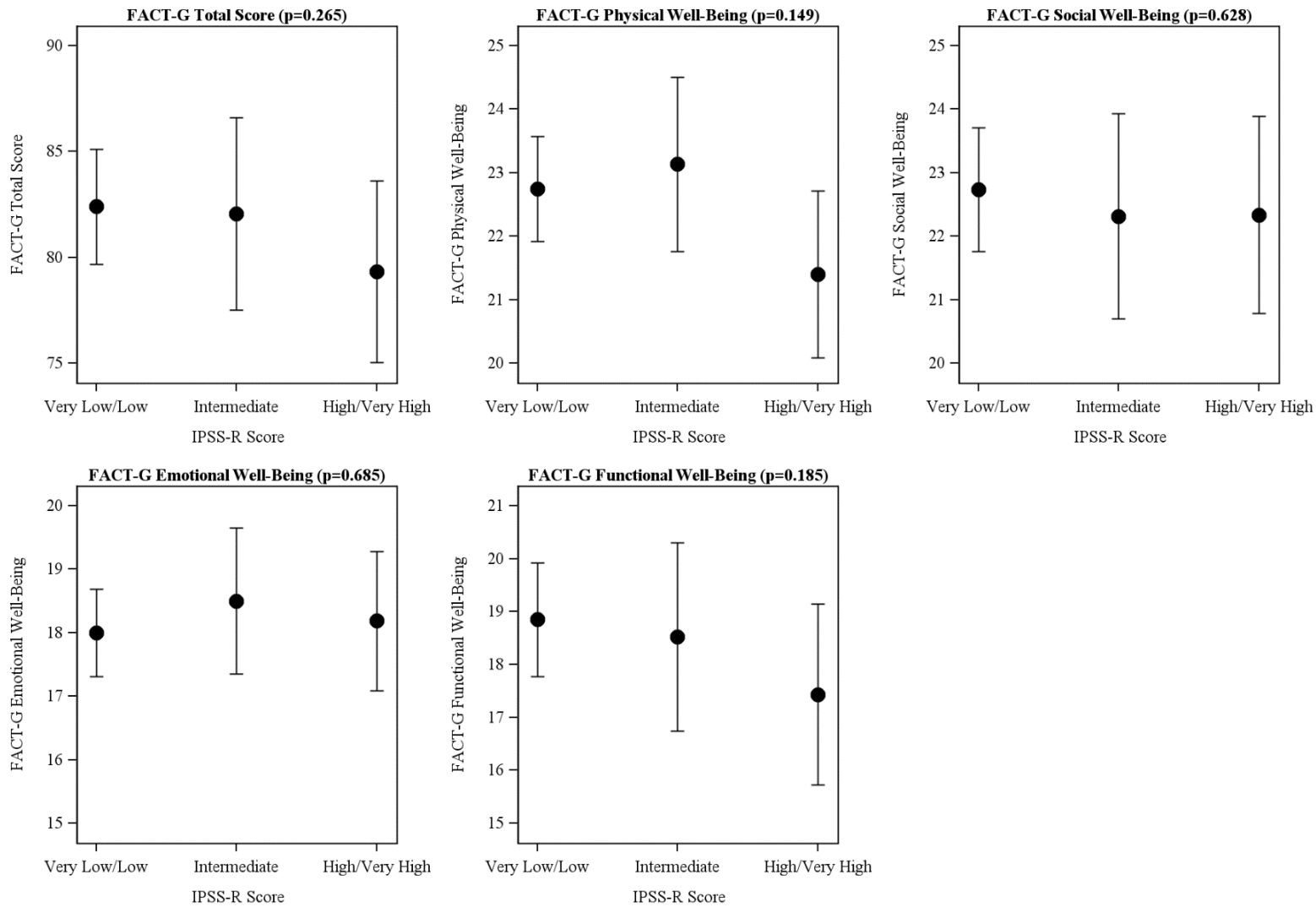
Number of participants (N) in each disease and vulnerability: Vulnerable MDS (N=84), MDS/MPN (N=18), ICUS (N=12), AML<30% (N=5), At-Risk (N=30), Non-Vulnerable MDS (N=164), MDS/MPN (N=22), ICUS (N=36), AML<30% (N=10), At-Risk (N=68). Estimates based on ANCOVA model adjusted for age. P-values for pairwise comparisons adjusted using the Hochberg procedure. Vulnerable defined as VES-13 \geq 3. HRQoL=Health-related quality of life. FACT-G=Functional Assessment of Cancer Therapy – General; VES-13=13-item Vulnerable Elders Survey.

Supplemental Figure 4: Summary of QALM Scores by IPSS-R Score in MDS or MDS/MPN Overlap



Number of participants (N) with MDS or MDS/MPN overlap in each IPSS-R Strata: Very Low/Low (N=149), Intermediate (N=54), High/Very High (N=58). Estimates based on ANCOVA model adjusted for age. Estimates and p-value based on linear regression of QoL score and IPSS-R score adjusted for age. HRQoL=Health-related quality of life. QALMS=Quality of Life in Myelodysplasia Scale.

Supplemental Figure 5: Summary of FACT-G Scores by IPSS-R Score in MDS or MDS/MPN Overlap



Number of participants (N) with MDS or MDS/MPN overlap in each IPSS-R Strata: Very Low/Low (N=149), Intermediate (N=54), High/Very High (N=58). Estimates based on ANCOVA model adjusted for age. Estimates and p-value based on linear regression of QoL score and IPSS-R score adjusted for age. HRQoL=Health-related quality of life. FACT-G=Functional Assessment of Cancer Therapy – General; Patient Reported Outcomes Measurement Information System=PROMIS Short-Form Fatigue; VES-13=13-item Vulnerable Elders Survey.