SUPPLEMENTARY MATERIALS

For the study:

Association of the Intermountain Risk Score with Major Adverse Health Events in Patients Positive for COVID-19: an Observational Evaluation of a US Cohort

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Supplemental Results

IMRS also predicted the need for ICU care (p-trend=0.001) and mechanical ventilation (p-trend=0.015) among subjects who were hospitalized (Table 2). It further predicted longitudinal incidence of coronary heart disease [p-trend<0.001, including n=15 with unstable angina and n=4 with MI, incident stroke (p-trend=0.008), incident deep vein thrombosis (p-trend<0.001), admission for atrial fibrillation (p<0.001), and admission for heart failure diagnosis or exacerbation (p<0.001)] (Table 2). BMP and CBC components that individually predicted the composite endpoint in Cox regression entering age, sex, and CBC and BMP components were glucose (quintile 5 vs. 1: HR=2.22, CI=1.55, 3.18, p<0.001), creatinine (quintile 5 vs. 1:HR=1.64, CI=1.14, 2.37), MCHC (quintile 1 vs. 5: HR=1.45, CI=0.98, 2.15, p=0.06), RDW (quintile 5 vs. 1: HR=1.70, CI=1.12, 2.57, p=0.013), and MPV (quintile 1 vs. 5: HR=1.88, CI=1.32, 2.67, p<0.001).

The strength of association of IMRS was reduced when controlling for comorbidities and risk factors; when entered in the Cox model first, IMRS reduced the -2 log likelihood for mortality by 105.6 more than when the comorbidities and risk factors were added before it. The Charlson index, male gender, obesity, hypertension, and smoking together reduced the -2 log likelihood by 143.3 when added to a model containing IMRS, but reduced it by 249.0 when added prior to adding IMRS. This modeling demonstrates that IMRS captured 42.4% (105.6/249.0) of the variance of those other factors. The Charlson index components that were most contributory in a model entering IMRS were MI (HR=1.31, CI=0.96, 1.79), cerebrovascular disease (HR=1.40, CI=1.07, 1.82), CKD (HR=1.46, CI=1.13, 1.89), moderate/severe liver disease (HR=0.47, CI=0.19, 1.14), and diabetes without complications (HR=1.60, CI=1.25, 2.03). The Charlson index also predicted COVID-19 hospitalization or mortality in Cox models entering IMRS in older and younger subjects. For older subjects, male gender, obesity, hypertension, hyperlipidemia, and diabetes without complications had a higher risk of hospitalization/mortality, and smoking history was associated with a lower risk. In the younger population, predictive factors beyond

IMRS were male gender, obesity, diabetes without complications, cancer, metastatic cancer, cerebrovascular disease, chronic kidney disease, and connective tissue disease.

Secondary population. Patients whose IMRS was calculated from CBC and BMP panels that were tested at the time of COVID-19 diagnosis (2020 cohort) included a total of n=2,014 subjects. Of these, 239 subjects (6.2%) were also included in the primary study population (the 2019 cohort). In the 2020 cohort, age averaged 52.7±19.1 years, 48.9% (n=984) were male, BMI was 31.6±8.7 kg/m^2, and IMRS categories of low, mild, moderate, and high risk consisted of 17.2%, 28.8%, 43.8%, and 10.2% of subjects, respectively. On average, the CBC and BMP laboratory panels were tested on the same day as COVID-19 diagnosis with a standard deviation of 1.8 days. IMRS measured in the 2020 cohort (Supplemental Figure S2) significantly stratified the composite of hospitalization or mortality. Absolute risks of the composite endpoint stratified by IMRS for the 2020 cohort are shown in Supplemental Table S4, with the relative hazards provided in Supplemental Table S5.

The area under the receiver operator characteristic curve had c-statistics for the primary composite endpoint in the 2020 cohort of c=0.606 for females and c=0.653 for males. The sensitivity, specificity, PPV, NPV, and accuracy are provided in Supplemental Table S6. For hospitalization and mortality separately, subjects in the 2020 cohort had c-statistics for females and males of, respectively, for hospitalization: c=0.562 and c=0.542, and, for mortality: c=0.825 and 0.875.

Supplemental Table S1. Baseline basic metabolic profile (BMP) and complete blood count (CBC) components across IMRS categories* of low, mild, moderate, and high-risk (2019 cohort).

Characteristic	Overall	Low IMRS	Mild IMRS	Moderate IMRS	High IMRS
BMP Components					
Sodium	139.1±2.5	139.5±1.9	139.1±2.4	138.6±2.9	137.8±3.7†
Chloride	105.9±3.0	106.3±2.3	105.8±2.9	105.4±3.6	105.3±4.7†
Potassium	4.05±0.42	4.04±0.39	4.06±0.42	4.04±0.47	4.12±0.51
Calcium	9.41±0.53	9.54±0.43	9.44±0.47	9.23±0.61	8.86±0.76†
Bicarbonate	23.9±2.8	24.0±2.6	24.0±2.6	23.8±3.2	23.2±3.8‡
Glucose	114±54	95±25	115±56	135±71	144±63†
Creatinine	0.95±0.86	0.83±0.20	0.88±0.48	1.08±1.31	1.76±2.22†
BUN	15.3±8.0	13.0±4.2	15.1±5.5	17.5±10.3	25.6±18.8†
CBC Parameters					
RBC count	4.74±0.63	4.89±0.50	4.87±0.56	4.49±0.70	3.83±0.73†
Hemoglobin	14.0±1.9	14.5±1.5	14.4±1.7	13.0±2.1	11.2±2.0†
Hematocrit	42.3±5.2	43.5±4.1	43.5±4.6	40.1±5.7	35.2±6.1†
WBC count	8.01±3.12	7.46±2.34	7.99±2.79	8.71±4.05	9.14±4.19†

Platelet count	260±78	267±70	259±71	253±90	254±120†
MCV	89.6±5.7	89.1±4.4	89.6±5.4	89.8±7.1	92.6±8.0†
MCH	29.5±2.3	29.7±1.8	29.6±2.2	29.1±2.8	29.5±3.0†
MCHC	33.0±1.4	33.3±1.1	33.1±1.4	32.4±1.5	31.8±1.3†
RDW	13.5±1.5	12.9±0.9	13.4±1.2	14.4±1.9	15.4±1.8†
RDW-SD	43.9±4.7	41.7±2.8	43.5±3.6	46.8±5.3	51.6±6.0†
MPV	10.3±1.0	10.3±1.0	10.4±1.0	10.4±1.0	10.4±1.1

*Categories of low, mild, moderate, and high risk were IMRS ≤5, 6-8, 9-14, and ≥15 for females and IMRS ≤6, 7-10, 11-16, ≥17 for males, respectively; †p-trend<0.001; ‡p-trend≤0.05 (and p-trend≥0.001).

Supplemental Table S2. Absolute risk in substrata across Intermountain Risk Score (IMRS) categories for the composite endpoint of hospitalization or mortality of patients testing positive for COVID-19 who had complete blood count (CBC) and basic metabolic profile (BMP) laboratory panels tested in 2019 (2019 cohort). For relative hazards, please see Table 3.

	Outcome Stratified by IMRS Risk Categories*				
Subgroup	**Overall**	**Low IMRS**	**Mild IMRS**	**Moderate IMRS**	**High IMRS**
Age ≥60 years	18.2% (198/1,087)	11.1% (9/81)	12.6% (47/373)	20.9% (107/513)	29.2% (35/120)
Age <60 years	5.5% (155/2,796)	3.0% (43/1,421)	6.9% (61/883)	9.7% (45/466)	23.1% (6/26)
Females	7.3% (170/2,329)	3.3% (34/1,018)	6.8% (43/629)	12.3% (74/600)	23.2% (19/82)
Males	11.8% (183/1,554)	3.7% (18/484)	10.4% (65/627)	20.6% (78/379)	34.4% (22/64)
Charlson tertile 1	3.5% (50/1,433)	2.5% (21/850)	4.9% (20/409)	4.7% (8/170)	25.0% (1/4)
Charlson tertile 2	7.6% (61/803)	5.5% (13/237)	7.5% (26/348)	9.7% (20/206)	16.7% (2/12)
Charlson tertile 3	20.6% (236/1,143)	13.2% (16/121)	16.7% (59/354)	22.7% (123/541)	29.9% (38/127)

*Categories of low, mild, moderate, and high risk were IMRS ≤5, 6-8, 9-14, and ≥15 for females and IMRS ≤6, 7-10, 11-16, ≥17 for males, respectively.

Supplemental Table S3. Relative hazards [hazard ratios (HR), 95% confidence intervals (CI)] for the association of the Intermountain Risk Score (IMRS) with the composite endpoint of hospitalization or mortality for patients in subpopulations of subjects who tested positive for COVID-19 and had complete blood count (CBC) and basic metabolic profile (BMP) panels measured in 2019 (2019 cohort).

Subpopulation	Mild IMRS vs. Low Risk	Moderate IMRS vs. Low Risk	High IMRS vs. Low Risk
Population Subgroups (all subgroup analyses are for the composite hospitalization/mortality outcome)‡			
Heart failure (n=338)	1.94 (0.55, 6.86)	2.34 (0.73, 7.55)	4.15 (1.23, 13.96)†
Cancer (n=321)	3.54 (0.79, 15.80)	7.35 (1.76, 30.62)†	10.67 (2.39, 47.70)†
Metastatic Cancer (n=56)	1.31 (0.15, 11.73)	1.76 (0.22, 14.34)	3.84 (0.43, 34.42)
Cerebrovascular dz (n=357)	1.00 (0.46, 2.17)	0.93 (0.44, 1.95)	2.51 (1.12, 5.64)†
Chronic pulmonary dz (n=1,423)	2.48 (1.48, 4.15)*	3.78 (2.30, 6.20)*	6.31 (3.39, 11.72)*
Diabetes, no complic. (n=872)	1.47 (0.79, 2.74)	1.75 (0.96, 3.19)	2.65 (1.33, 5.31)†
Diabetes, complic. (n=366)	1.46 (0.44, 4.86)	1.92 (0.60, 6.13)	2.49 (0.74, 8.43)
Chronic kidney dz (n=417)	1.58 (0.62, 4.00)	2.28(0.99, 5.25)	3.42 (1.40, 8.37)†
Mild liver disease (n=638)	1.25 (0.68, 2.30)	1.30 (0.72, 2.35)	2.87 (1.33, 6.18)†
Peptic ulcer disease (n=241)	4.82 (0.58, 40.04)	13.65 (1.82, 102.28)†	19.33 (2.42, 154.59)†
Dementia (n=105)	0.25 (0.02, 3.93)	0.93 (0.12, 7.01)	1.37 (0.17, 10.80)
PVD (n=343)	4.10 (0.96, 17.56)	3.65 (0.88, 15.07)	5.01 (1.15, 21.93)†

Paralysis (n=72)	0.29 (0.03, 2.79)	1.66(0.45, 6.12)	0.76 (0.08, 7.27)
Connective tissue dz (n=141)	0.90 (0.27, 2.96)	1.47 (0.57, 3.78)	4.02 (1.29, 12.49)†
Obesity (n=1,635)	1.94 (1.28, 2.94)†	2.97 (1.99, 4.43)*	4.81 (2.40, 8.37)*
Hypertension (n=1,622)	1.71 (1.04, 2.80)†	2.78 (1.73, 4.44)*	4.70 (2.73, 8.07)*
Hyperlipidemia (1,412)	2.16 (1.25, 3.72)†	3.23 (1.91, 5.46)*	5.29 (2.88, 9.71)*
Smoking history (n=1,102)	3.03 (1.49, 6.14)†	4.49 (2.27, 8.88)*	9.85 (4.26, 22.81)*
Coronary artery dz (n=557)	3.43 (1.05, 11.26)†	4.65(1.46, 14.80)†	7.43 (2.23, 24.74)†
Depression (n=1,396)	2.03 (1.22, 3.38)†	4.11 (2.59, 6.54)*	7.48 (4.19, 13.34)*
PCI history (n=118)	2.25 (0.28, 17.73)	3.41 (0.45, 25.63)	4.91 (0.59, 40.85)

*p<0.001; †p≤0.05 (and p≥0.001); ‡Results for subjects with a history of MI (n=206), moderate/severe liver disease (n=30), HIV/AIDS (n=3), AF (n=258), and CABG (n=42) are not provided because no events occurred in the low risk group.

Supplemental Table S4. Absolute risk across Intermountain Risk Score (IMRS) categories of the composite of hospitalization or mortality and of hospitalization alone and mortality alone for patients testing positive for COVID-19 who had complete blood count (CBC) and basic metabolic profile (BMP) measured in 2020 at the time of COVID-19 diagnosis (2020 cohort).

		Outcome Stratified by IMRS Risk Categories*			
Endpoint	**Overall Outcome**	**Low IMRS**	**Mild IMRS**	**Moderate IMRS**	**High IMRS**
Hospitalization/Mortality	12.2% (246/2,014)	7.8% (27/346)	7.4% (43/580)	13.7% (121/883)	26.8% (55/205)
Hospitalization only	9.4% (189/2,014)	7.8% (27/346)	7.2% (42/580)	10.3% (91/883)	14.1% (29/205)
Mortality only	3.3% (67/2,014)	0% (0/346)	0.2% (1/580)	3.9% (34/883)	15.6% (32/205)

*Low, mild, moderate, and high-risk categories were IMRS ≤5, 6-8, 9-14, and ≥15 for females and ≤6, 7-10, 11-16, ≥17 for males, respectively.

Supplemental Table S5. Relative hazards [hazard ratios (HR), 95% confidence intervals (CI)] for the association of the Intermountain Risk Score (IMRS) with the composite endpoint of hospitalization or mortality (and with each endpoint separately) for the 2020 cohort.

Outcome/Population	Mild Risk vs. Low Risk	Moderate Risk vs. Low Risk	High Risk vs. Low Risk
Hospitalization/Mortality	0.84 (0.52, 1.35)	1.36 (0.90, 2.07)	2.75 (1.73, 4.36)*
Hospitalization only	0.81 (0.50, 1.32)	1.02 (0.66, 1.57)	1.43 (0.85, 2.42)
Mortality only	NR‡	NR‡	NR‡

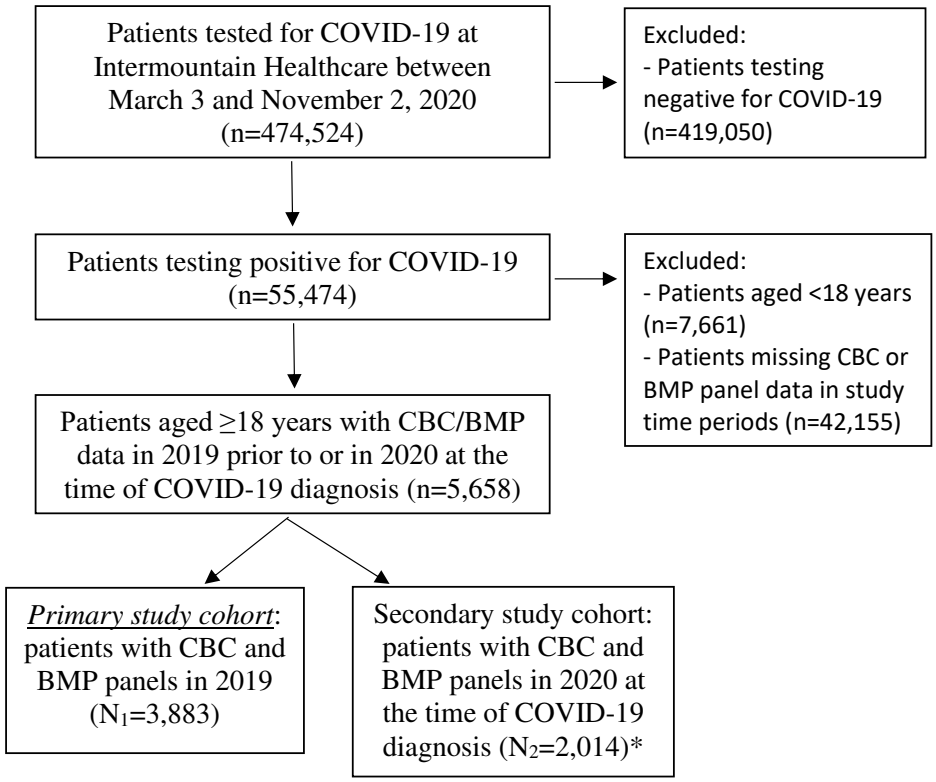
*p<0.001; †p≤0.05 (and p≥0.001); ‡NR: Not reported because mortality was 0% in the low-risk referent category and, thus, statistical comparisons to that group could not be performed.

Supplemental Table S6. Predictive values for analyses in the primary 2019 cohort and in the 2020 cohort for: 1) the high-risk IMRS group compared to the combination of low, mild, and moderate-risk IMRS and 2) the grouping of high and moderate-risk IMRS compared to low and mild-risk IMRS.

Population	Sensitivity	Specificity	PPV	NPV	Accuracy
2019 cohort (N=3,883):					
High-risk IMRS*	11.6%	97.0%	28.1%	94.2%	89.3%
High/Moderate-risk IMRS†	54.7%	73.6%	17.2%	91.7%	71.9%
2020 cohort (N=2,014):					
High-risk IMRS*	22.4%	91.5%	26.8%	92.4%	83.1%
High/Moderate-risk IMRS†	71.5%	48.4%	16.2%	89.4%	51.2%

*Referent is subjects in low, mild, and moderate-risk IMRS categories; †Referent is subjects in low and mild-risk IMRS categories.

Supplemental Figure S1. CONSORT-style flow diagram.



*n=239 of these N_2=2,014 patients were included in the N_1=3,883 subjects of the primary 2019 study cohort.

Supplemental Figure S2. Kaplan-Meier survival curves demonstrating the association of IMRS with the composite endpoint of hospitalization or mortality in the 2020 cohort whose CBC and BMP panels were tested at that time of COVID-19 diagnosis (N=2,014). Categories of low, mild, moderate, and high risk correspond, respectively, to IMRS ≤5, 6-8, 9-14, and ≥15 for females and IMRS ≤6, 7-10, 11-16, ≥17 for males.