Table S1 –Definitions of Comorbidities

Comorbidity	HCT-CI Definition	SCI Definition
Arrhythmia	Atrial fibrillation or flutter, sick sinus syndrome, or ventricular arrhythmias	**Composite cardiac disease/dysfunction** - Any condition included falling under the definition arrhythmia, cardiac, or heart valve disease in the HCT-CI
Cardiac	Coronary artery disease, congestive heart failure, history of myocardial infarction, or left ventricular ejection fraction $\leq$ 50%	
Heart valve disease	Except mitral valve prolapse	
Diabetes Mellitus	Diabetes Mellitus requiring treatment with insulin or hypoglycemic agents at the time of initiation of conditioning	Not included
Mild Hepatic	Serum bilirubin between ULN and 1.5 times ULN; ALT or AST between ULN and 2.5 times ULN, or chronic hepatitis	**Moderate to severe hepatic dysfunction** – only moderate to severe hepatic comorbidity qualify as a hepatic comorbidity by the SCI
Moderate/Severe Hepatic	Serum bilirubin greater than 1.5 times ULN; ALT or AST greater than 2.5 times ULN, or chronic hepatitis	
Infection	Infection requiring antimicrobial therapy continuing after the date of transplantation (day 0)	Not included
Obesity	Body mass index $\geq$ 35 kg/m^2	Not included
Psychiatric	Depression or anxiety which requires treatment at the time of transplantation	Not included
Moderate Pulmonary	DLCo[a] or FEV$_1$ 66-80% or dyspnea on slight activity	**Identical criteria**
Severe Pulmonary	DLCo[a] or FEV$_1$ < 66 or dyspnea at rest/oxygen dependent	**Identical criteria**
Moderate/severe renal	Serum creatinine > 2 mg/dL, on dialysis, or prior renal transplantation	**Renal dysfunction** was defined according to estimated glomerular filtration rate (eGFR) mL/min/ 1.73 m2, using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula for estimating creatinine clearance. A eGFR $\geq$ 90 ml/min/1.73 m2 was considered normal, between 60 to 89.9 ml/min/1.73 m2 mildly decreased, and below 60 ml/min/1.73 m2 moderately to severely decreased
Cerebrovascular disease	Transient ischemic attack or cerebrovascular accident	Not included
Rheumatologic	SLE, RA, polymyositis, mixed CTD, or polymyalgia rheumatica	Not included

Prior malignancy	Malignancy unrelated to the indication for transplantation which has been treated at any point in the patient's history, excluding non-melanoma skin cancer	Not included
Peptic ulcer	Requiring treatment	Not included
Inflammatory bowel disease	Crohn disease or ulcerative colitis	Not included

ULN – upper limit of normal; ALT – alanine aminotransferase; AST – aspartate aminotransferase; DLCo – diffusion capacity of the lung for carbon monoxide; FEV_1 – forced expiratory volume in one second; DLco, diffusion capacity of carbon monoxide; SLE – systemic lupus erythmatosis; RA – rheumatoid arthritis; CTD – connective tissue disease

[a] DLCo corrected for hemoglobin using the Cotes formula as per institutional standard

Table S2 –Comparison of population characteristics by HCT-CI

		HCT-CI 0-3	HCT-CI ≥ 4	
Recipient age, years (median [IQR])		54 [43, 62]	58 [51, 65]	<0.001
	Age < 60	234 (67)	124 (55)	0.005
	Age ≥ 60	114 (33)	101 (45)	
Recipient sex (%)	Male	201 (58)	128 (57)	0.905
	Female	147 (42)	97 (43)	
Karnofsky Performance Status (%)	90-100	243 (70)	122 (54)	<0.001
	<90	104 (30)	103 (46)	
Recipient CMV serostatus (%)	absent	133 (38)	89 (40)	0.816
	present	215 (62)	136 (60)	
Diagnosis (%)	Acute myeloid leukemia	135 (39)	82 (36)	0.395
	Myelodysplastic syndrome	66 (19)	59 (26)	
	Multiple myeloma	72 (21)	43 (19)	
	Acute lymphoblastic leukemia	35 (10)	22 (10)	
	Myeloproliferative neoplasm	21 (6)	10 (4)	
	Chronic myeloid leukemia	13 (4)	4 (2)	
	Other leukemia	6 (2)	5 (2)	
CIBMTR disease risk (%)	low/intermediate	231 (66)	156 (69)	0.589
	high	86 (25)	54 (24)	
	unclassifiable	31 (9)	15 (7)	
Month from Dx to HCT (median [IQR])		7 [4, 24]	8 [5, 26]	0.357
Donor/recipient sex (%)	Female/male			
	other			
Donor type* (%)	Matched related	119 (34)	73 (32)	0.455
	Matched unrelated	175 (50)	108 (48)	
	HLA Mismatched	54 (16)	44 (20)	
HCT year (median [IQR])		2014 [2012, 2016]	2013 [2012, 2016]	0.141
Regimen (%)	Melphalan-based	246 (71)	190 (84)	<0.001
	TBI-based	102 (29)	35 (16)	

IQR – interquartile range; HCT-CI – hematopoietic cell transfer comorbidity index; CMV – cytomegalovirus; CIBTMR – center for international bone and marrow transplantation; Dx- diagnosis; HCT – hematopoietic cell transplantation; TBI – total body irradiation

Table S3 –Cox Multivariable Regression for non-relapse mortality and overall survival in the Memorial Sloan Kettering cohort

	Non-relapse mortality		Overall survival	
	HR (95% CI)	P-value	HR (95% CI)	P-value
SCI score				
0		Reference		
1	3.39 (0.92-12.41)	0.066	1.64 (0.74-3.65)	0.223
2	6.7 (1.83-24.58)	0.004	3.28 (1.49-7.23)	0.003
3	7.64 (1.92-30.39)	0.004	3.1 (1.23-7.82)	0.016
≥ 4	7.95 (1.44-43.71)	0.017	3.41 (0.85-13.6)	0.083
Regimen				
Melphalan-based		Reference		
TBI-based	0.61 (0.22-1.71)	0.349	0.92 (0.45-1.86)	0.812
Karnofsky performance status				
≤ 80		Reference		
90 -100	0.71 (0.34-1.49)	0.368	0.57 (0.33-1)	0.048
CIBMTR Disease Risk				
Low/Intermediate		Reference		
High	0.87 (0.37-2.08)	0.758	1.18 (0.61-2.27)	0.622
Unclassifiable	0.77 (0.26-2.24)	0.629	0.79 (0.3-2.05)	0.623
Recipient CMV serostatus				
Negative		Reference		
Positive	0.84 (0.4-1.74)	0.634	1.13 (0.64-2)	0.665
Donor type				
Matched related		Reference		
Matched unrelated	1.27 (0.59-2.74)	0.549	1.12 (0.63-1.99)	0.702
Mismatched	2.39 (0.82-6.97)	0.109	1.81 (0.76-4.34)	0.181
Acute GvHD grade*				
0 - 1		Reference		
≥ 2	2.28 (1.12-4.66)	0.024	2.07 (1.16-3.68)	0.014

* Time-dependent covariate

CI – confidence interval; HR – hazard ratio; SCI – simplified comorbidity index; EBMT – European Society for Blood and Marrow Transplantation; CMV - cytomegalovirus CMV – cytomegalovirus; GvHD – graft-versus host disease

Table S4- Non-relapse mortality discrimination of the Simplified Comorbidity Index (SCI) with and without age

Years post HCT	MSKCC cohort		Sheba cohort	
	SCI original AUC (95% CI)	**SCI without age** AUC (95% CI)	**SCI original** AUC (95% CI)	**SCI without age** AUC (95% CI)
1	70.3 (64.4 - 76.1)	68.1 (62.1 - 74.1)	72.0 (62.0-76.5)	70.1 (62.1, 78.1)
2	68.9 (63.3 - 74.4)	66.4 (60.6 - 72.2)	67.6 (57.4-77.9)	64.4 (55.3, 73.5)
3	68.7 (63.1 - 74.4)	67.0 (61.2 - 72.7)	64.9 (54.1-75.7)	64.0 (53.1, 74.8)
4	67.5 (61.6 - 73.5)	66.4 (60.5 - 72.4)	61.8 (64.4, 79.7)	64.7 (51.7, 77.7)

HCT – hematopoietic cell transplantation (HCT); AUC – area under the receiver operating characteristic curve

Table S5 – Multivariable Hazard Ratios for non-relapse mortality and overall survival in the Sheba Cohort

	Non-relapse mortality		Overall mortality	
	HR (95% CI)	**P-value**	**HR (95% CI)**	**P-value**
SCI score				
0-1		*Reference*		
2	1.90 (0.60, 6.06)	0.276	1.10 (0.57, 2.13)	0.775
3	3.70 (1.34, 10.19)	0.011	1.51 (0.85, 2.69)	0.159
≥ 4	5.67 (2.12, 15.16)	0.001	2.23 (1.30, 3.84)	0.004
Regimen				
Flu + Treo 36-42 g/m²		*Reference*		
Flu + Treo 30 g/m²	0.75 (0.34, 1.67)	0.479	1.24 (0.74, 2.06)	0.413
Flu + Melphalan 100 mg/m²	0.85 (0.32, 2.25)	0.744	0.94 (0.49, 1.82)	0.858
Flu + Melphalan 140 mg/m²	1.87 (0.70, 4.97)	0.210	1.07 (0.46, 2.52)	0.875
Karnofsky performance status				
≤ 80		*Reference*		
90 -100	0.32 (0.16, 0.64)	0.001	0.37 (0.22, 0.62)	< 0.001
EBMT Disease Risk				
Low/Intermediate		*Reference*		
High	0.83 (0.47, 1.45)	0.503	0.85 (0.58, 1.25)	0.404
Recipient CMV serostatus				
Negative		*Reference*		
Positive	1.11 (0.55, 2.25)	0.762	1.25 (0.76, 2.05)	0.383
Donor type				
Matched related		*Reference*		
Matched unrelated	2.25 (1.08, 4.71)	0.031	1.54 (0.88, 2.70)	0.133
Mismatched	1.15 (0.61, 2.16)	0.665	1.02 (0.67, 1.55)	0.931

CI – confidence interval; HR – hazard ratio; SCI – simplified comorbidity index; Flu – fludarabine; Treo – treosulfan; EBMT – European Society for Blood and Marrow Transplantation; CMV - cytomegalovirus CMV – cytomegalovirus

Table S6 –Cox Multivariable Regression for non-relapse mortality and overall survival in the Sheba cohort

	Non-relapse mortality		Overall survival	
	HR (95% CI)	P-value	HR (95% CI)	P-value
SCI score				
0-1		*Reference*		
2	1.45 (0.45, 4.66)	0.535	1.00 (0.52, 1.95)	0.989
3	3.77 (1.36, 10.46)	0.011	1.50 (0.84, 2.68)	0.171
≥ 4	4.86 (1.82, 12.99)	0.002	2.15 (1.25, 3.69)	0.006
Regimen				
Fludarabine-treosulfan 36 mg/m^2		*Reference*		
Fludarabine-treosulfan 30 mg/m^2	0.56 (0.25, 1.27)	0.164	1.09 (0.66, 1.82)	0.733
Flu + Melphalan 100 mg/m^2	0.73 (0.27, 1.97)	0.536	0.93 (0.48, 1.80)	0.823
Flu + Melphalan 140 mg/m^2	2.22 (0.84, 5.87)	0.110	1.16 (05.0, 2.74)	0.727
Karnofsky performance status				
≤ 80		*Reference*		
90 -100	0.28 (0.14, 0.57)	< 0.001	0.36 (0.21, 0.61)	< 0.001
CIBMTR Disease Risk				
Low/Intermediate		*Reference*		
High	0.78 (0.58, 1.05)	0.096	0.85 (0.69, 1.03)	0.101
Recipient CMV serostatus				
Negative		*Reference*		
Positive	0.96 (0.47, 1.95)	0.913	1.18 (0.72, 1.94)	0.514
Donor type				
Matched related		*Reference*		
Matched unrelated	1.13 (0.60, 2.15)	0.701	1.02 (0.67, 1.55)	0.934
Mismatched	1.61 (0.76, 3.44)	0.216	1.27 (0.72, 2.26)	0.410
Acute GvHD grade*				
0 - 1		*Reference*		
≥ 2	6.87 (3.43, 13.76)	< 0.001	2.42 (1.51, 3.88)	< 0.001

* Time-dependent covariate

CI – confidence interval; HR – hazard ratio; SCI – simplified comorbidity index; EBMT – European Society for Blood and Marrow Transplantation; CMV - cytomegalovirus CMV – cytomegalovirus; GvHD – graft-versus host disease