Allogeneic hematopoietic stem cell transplantation in patients aged 60-79 years in Germany (1998-2018): a registry study

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Received: March 20, 2023.
Accepted: August 11, 2023.
Early view: August 31, 2023.

https://doi.org/10.3324/haematol.2023.283175

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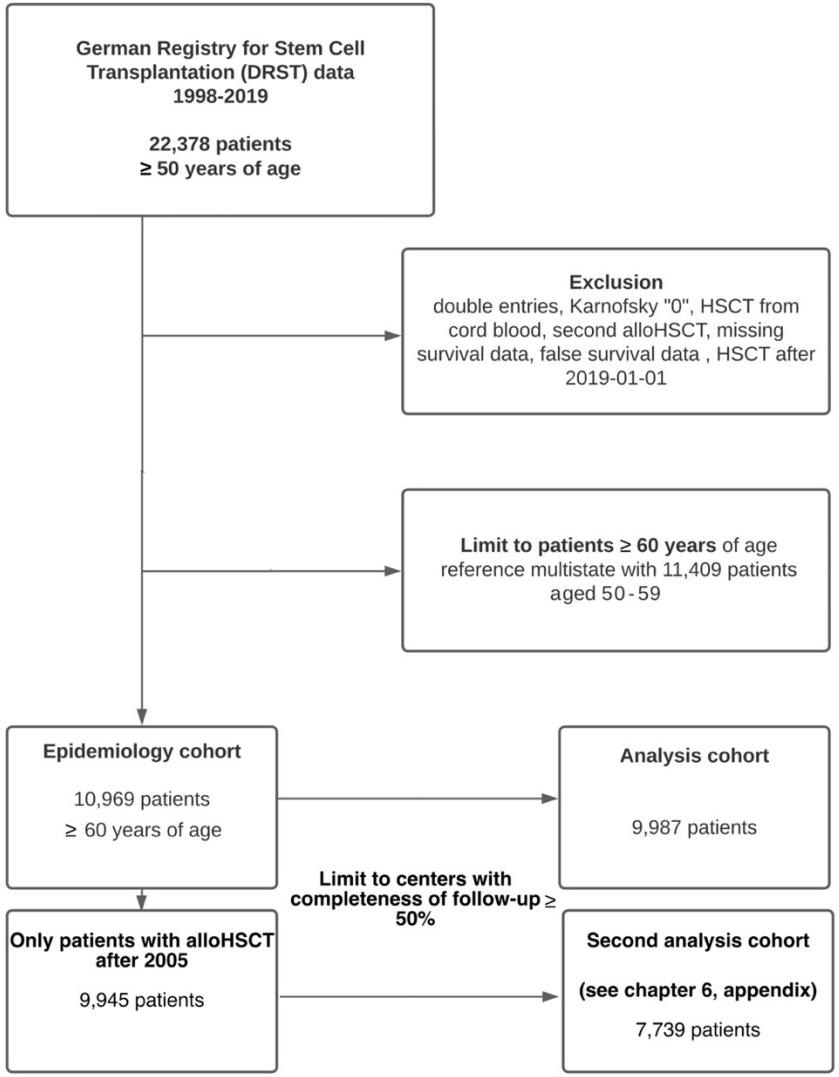


Supplemental table 1 – Conditioning Regimen and TCI

Bu Busulfane, Cy Cyclophosphamide, Flu Fludarabine, Mel Melphalane, TT Thiotepa, TBu(3/2)F = Busulfan 3/2 days, Thiotepa 5 mg/kg, Treo Treosulfane

Conditioning regimen & TCI values			
Variable	**N**	**60-69, N = 9,422**	**70-79, N = 1,547**
Conditioning regimen	10,969		
Bu(dose missing)Flu		648 (6.9%)	135 (8.7%)
Bu/Cy		139 (1.5%)	10 (0.6%)
Bu2Flu		1,310 (14%)	295 (19%)
Bu3Flu		185 (2.0%)	15 (1.0%)
Bu4Flu		23 (0.2%)	1 (<0.1%)
FBM (Flu/BCNU/Mel)		1,104 (12%)	212 (14%)
FLAMSA+other		1,155 (12%)	193 (12%)
Flu+Others		95 (1.0%)	6 (0.4%)
FluCy		275 (2.9%)	37 (2.4%)

Conditioning regimen & TCI values			
Variable	**N**	**60-69, N = 9,422**	**70-79, N = 1,547**
FluMel(dose missing)		337 (3.6%)	37 (2.4%)
FluMel110		27 (0.3%)	8 (0.5%)
FluMel140		354 (3.8%)	42 (2.7%)
FluTBI2Gy		1,087 (12%)	233 (15%)
FluTT		260 (2.8%)	44 (2.8%)
Others/not fully reported		986 (10%)	56 (3.6%)
TBI(dose missing)/Cy		47 (0.5%)	6 (0.4%)
TBI12/Cy		27 (0.3%)	0 (0%)
TBI12/VP16/CY		1 (<0.1%)	0 (0%)
TBI8/Cy		14 (0.1%)	0 (0%)
TBu2Flu		40 (0.4%)	10 (0.6%)
TBu3Flu		15 (0.2%)	0 (0%)
Treo36Flu		1,293 (14%)	207 (13%)
Total conditioning intensity - values[+]	8,616		

Conditioning regimen & TCI values			
Variable	**N**	**60-69, N = 9,422**	**70-79, N = 1,547**
1		275 (3.8%)	37 (2.8%)
1.5		2,684 (37%)	580 (44%)
2		40 (0.5%)	10 (0.8%)
2.5		1,832 (25%)	264 (20%)
3		2,288 (31%)	405 (31%)
3.5		23 (0.3%)	1 (<0.1%)
4		166 (2.3%)	10 (0.8%)
4.5		1 (<0.1%)	0 (0%)
Unknown		2,113	240

DRST Data								
Characteristic	60-69, N = 9422				70-79, N = 1547			
	N	1998-2008, N = 2,217[1]	2009-2018, N = 7,205[1]	p-value[2]	N	1998-2008, N = 112[1]	2009-2018, N = 1,435[1]	p-value[2]
Patient Sex	9,420			0.8	1,545			0.6
female		881 (40%)	2,839 (39%)			37 (33%)	508 (35%)	
male		1,336 (60%)	4,364 (61%)			75 (67%)	925 (65%)	
Patient Age	9,422	63.69 (61.79, 65.81)	64.37 (62.24, 66.90)	<0.001	1,547	71.25 (70.50, 73.11)	72.09 (70.91, 73.64)	0.001
Diagnosis	9,422			<0.001	1,547			0.3
Acute leukemia		1,197 (54%)	3,789 (53%)			80 (71%)	934 (65%)	
CLL		115 (5.2%)	240 (3.3%)			0 (0%)	37 (2.6%)	
CML		99 (4.5%)	76 (1.1%)			2 (1.8%)	10 (0.7%)	

Lymphoma		141 (6.4%)	646 (9.0%)			3 (2.7%)	60 (4.2%)	
MDS/MPN		431 (19%)	1,867 (26%)			25 (22%)	343 (24%)	
Others		77 (3.5%)	213 (3.0%)			2 (1.8%)	37 (2.6%)	
Plasma cell disorders		157 (7.1%)	374 (5.2%)			0 (0%)	14 (1.0%)	
Donor/Patient HLA-match	4,043			0.9	516			0.5
match		1,327 (86%)	2,150 (86%)			59 (88%)	382 (85%)	
mismatch		214 (14%)	352 (14%)			8 (12%)	67 (15%)	
Donor/Patient Relation	9,407			<0.001	1,545			<0.001
Family		739 (33%)	1,578 (22%)			30 (27%)	190 (13%)	
Unrelated		1,472 (67%)	5,618 (78%)			82 (73%)	1,243 (87%)	
Donor Age	4,310	42 (32, 58)	36 (27, 49)	<0.001	790	40 (31, 65)	34 (27, 44)	0.001
Stem cell source	9,409			>0.9	1,541			0.014

Bone marrow		119 (5.4%)	383 (5.3%)		0 (0%)	74 (5.2%)	
PBSC		2,095 (95%)	6,812 (95%)		112 (100%)	1,355 (95%)	
GvHD-Prophylaxis	8,655			<0.001	1,517		<0.001
CNI+MMF		701 (46%)	4,337 (61%)		46 (49%)	948 (67%)	
CsA+MTX		389 (25%)	1,878 (26%)		10 (11%)	266 (19%)	
Other		442 (29%)	908 (13%)		37 (40%)	210 (15%)	
TCI - Category	7,309			0.002	1,307		0.005
high		41 (3.3%)	126 (2.1%)		1 (1.2%)	9 (0.7%)	
int		654 (53%)	3,489 (57%)		56 (67%)	614 (50%)	
low		532 (43%)	2,467 (41%)		26 (31%)	601 (49%)	
Karnofsky Performance Index	7,970			0.002	1,415		0.041
< 80		127 (11%)	535 (7.9%)		13 (17%)	122 (9.1%)	

80		334 (28%)	1,814 (27%)			27 (35%)	410 (31%)		
90-100		727 (61%)	4,433 (65%)			38 (49%)	805 (60%)		
Relevant Comorbidities	4,897	301 (62%)	2,804 (64%)	0.6	980	35 (78%)	645 (69%)	0.2	
CMV relation	8,483			<0.001	1,494			0.015	
Both negative		375 (26%)	1,862 (26%)			25 (27%)	385 (27%)		
Both positive		549 (38%)	3,042 (43%)			28 (30%)	615 (44%)		
Negative Patient, positive Donor		156 (11%)	581 (8.2%)			12 (13%)	104 (7.4%)		
Positive Patient, negative Donor		350 (24%)	1,568 (22%)			28 (30%)	297 (21%)		
Disease status at HSCT - only CR	8,954	644 (31%)	2,534 (37%)	<0.001	1,489	32 (29%)	528 (38%)	0.040	
Disease status at HSCT	8,954			<0.001	1,489			<0.001	
1st CR		463 (22%)	2,018 (29%)			25 (22%)	386 (28%)		

Any other CR		181 (8.6%)	516 (7.5%)	7 (6.2%)	142 (10%)
Any partial Remission		249 (12%)	1,041 (15%)	2 (1.8%)	170 (12%)
Any R/R		609 (29%)	1,701 (25%)	53 (47%)	403 (29%)
Other		351 (17%)	926 (14%)	11 (9.8%)	173 (13%)
Untreated		255 (12%)	644 (9.4%)	14 (12%)	103 (7.5%)
Unknown		109	359	0	58

[1] n (%); Median (IQR)

[2] Pearson's Chi-squared test; Wilcoxon rank sum test; Fisher's exact test

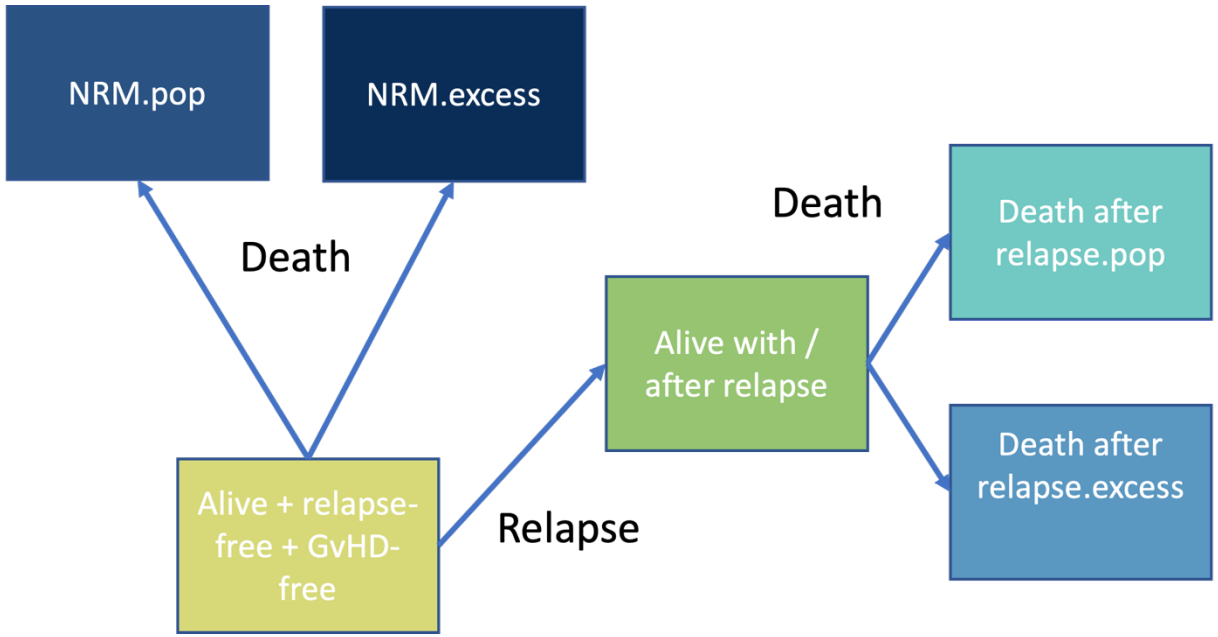
Supplemental table 2 – Demographic and Clinical Characteristics of the Patients at transplantation. Values per decade of transplant. IQR denotes interquartile range, HLA *human leukocyte antigen system, PBSC peripheral blood stem cell, MAC myeloablative conditioning, RIC reduced-intensity conditioning, CsA Ciclosporin A, MMF Mycophenolate mofetil, Tac Tacrolimus, TBI total body irradiation, CMV cytomegaly virus*

1. Multistate and Relative Survival

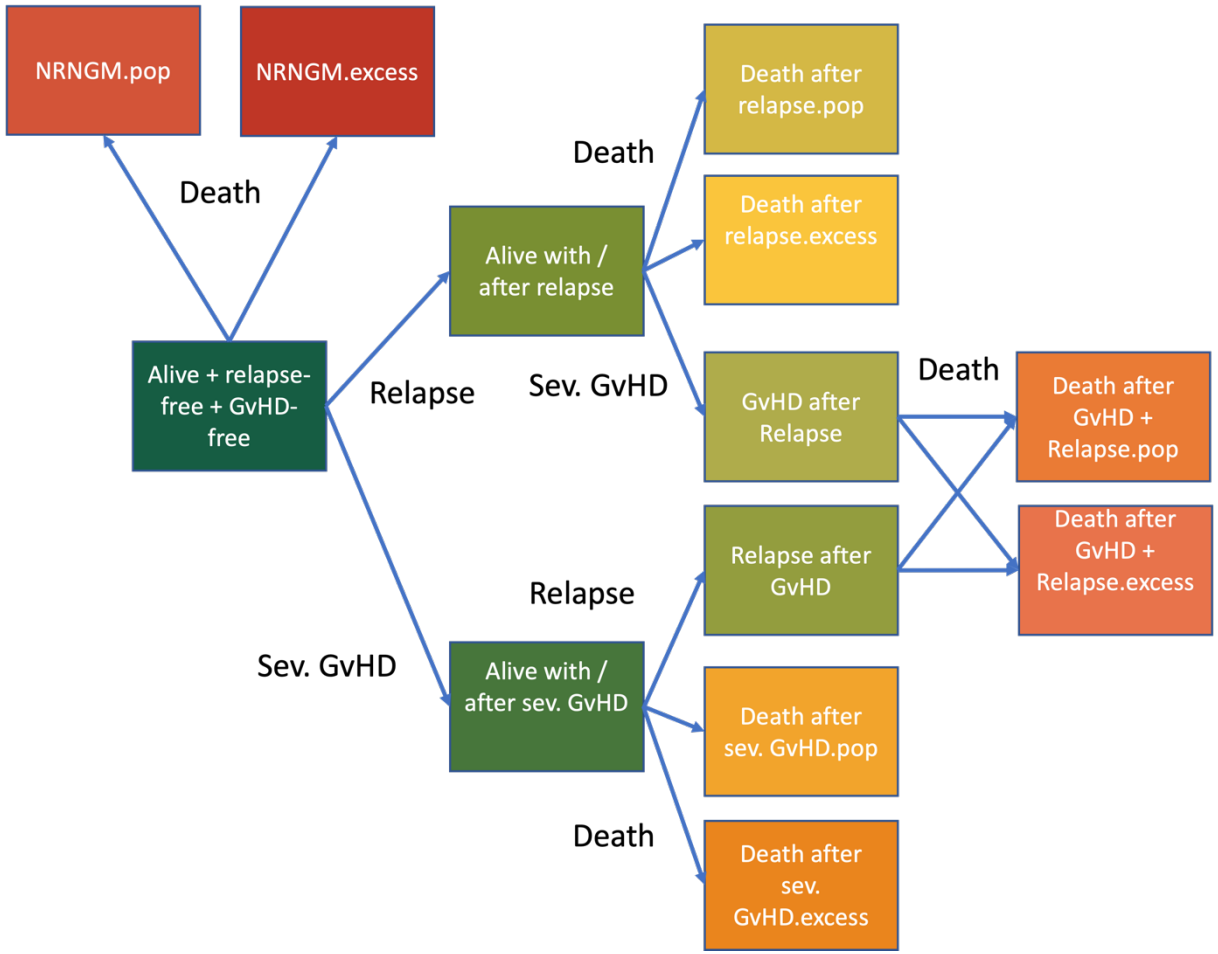
Multistate – Schematic Representation

Supplemental figure 2.1 Schematic representation of multistate models with different split-states.

Colors of different states fit to final figure color in RFS environment. Comparison to a German population to divide death events into population (.pop) or excess events.



Supplemental figure 2.2 Schematic representation of multistate models with different split-states.
Colors of different states fit to final figure color in GRFS environment. Comparison to a German population to divide death events into population (.pop) or excess events.

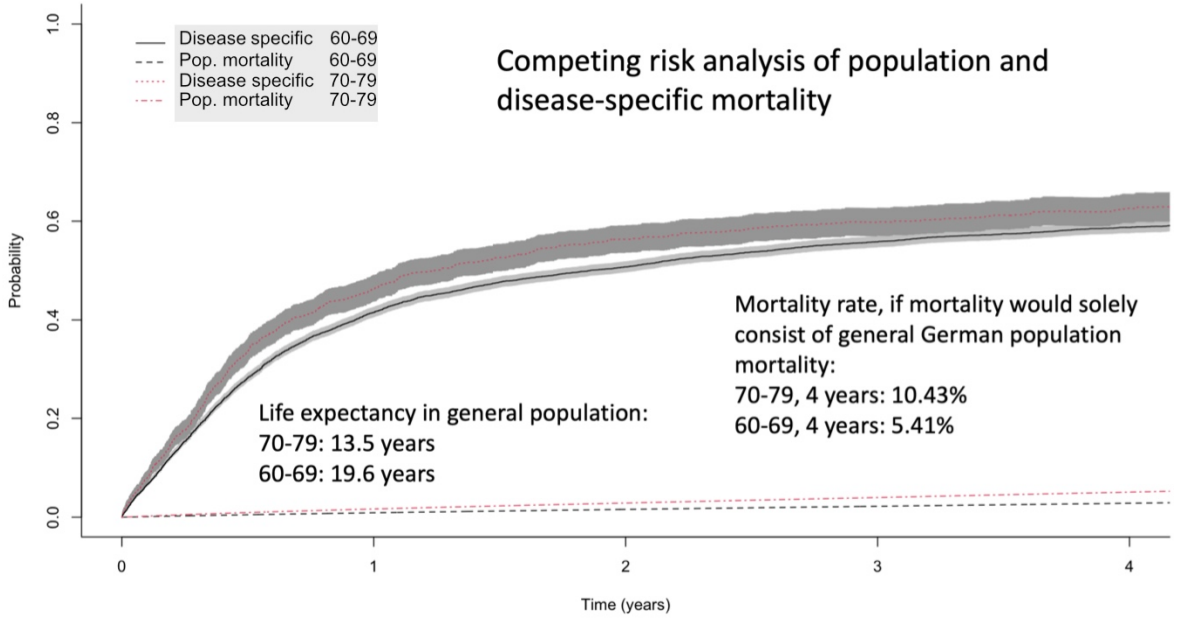


Sup 1: Additive Model – reference

Please refer to the relsurv vignette for an explanation of the additive model. https://cran.r-project.org/web/packages/relsurv/relsurv.pdf

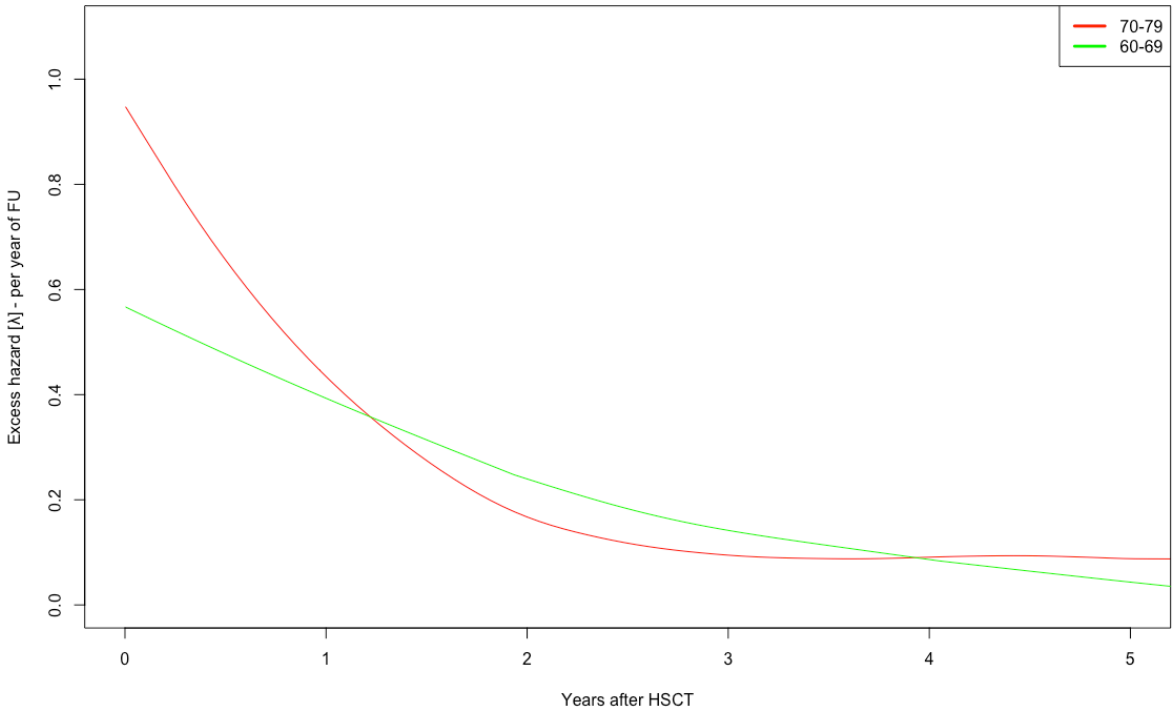
Supplemental figure 3 Competing risks of population mortality and disease-specific mortality without multistate integration.

Population data of underlying deathrate-tables of the German population 1998-2018. Importantly, due to competing risks analysis and disease-related death as a competing event the probability of population mortality within the HSCT cohort is lower than in the general population (lower right, 4-year mortality). Plainly, disease is causing a loss of lifetime that would be needed for population mortality to become the reason for death. Please compare the calculated 4-year values to values in table A1.1 and A1.2.

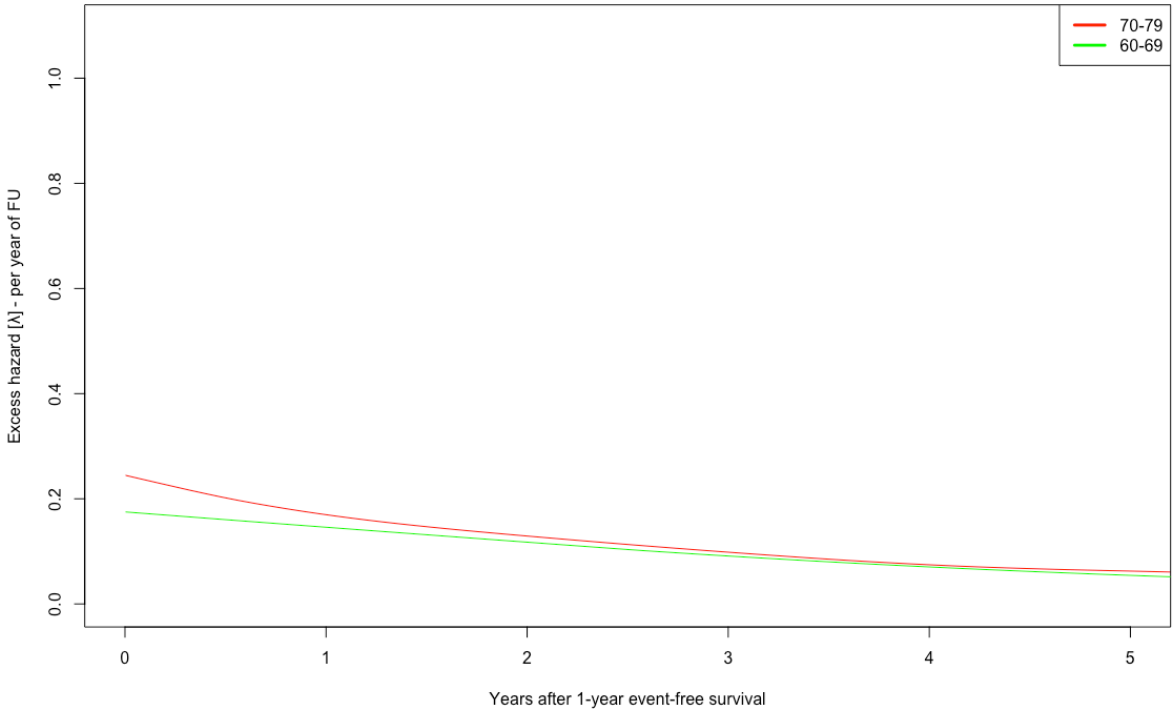


Excess mortality hazard

Supplemental figure 4.1. Excess mortality hazard in comparison to German general population (age-, sex- and year-matched). Epanechnikov kernel smoothing was obtained via relsurv package in R. *Refer to:* https://rdrr.io/cran/relsurv/

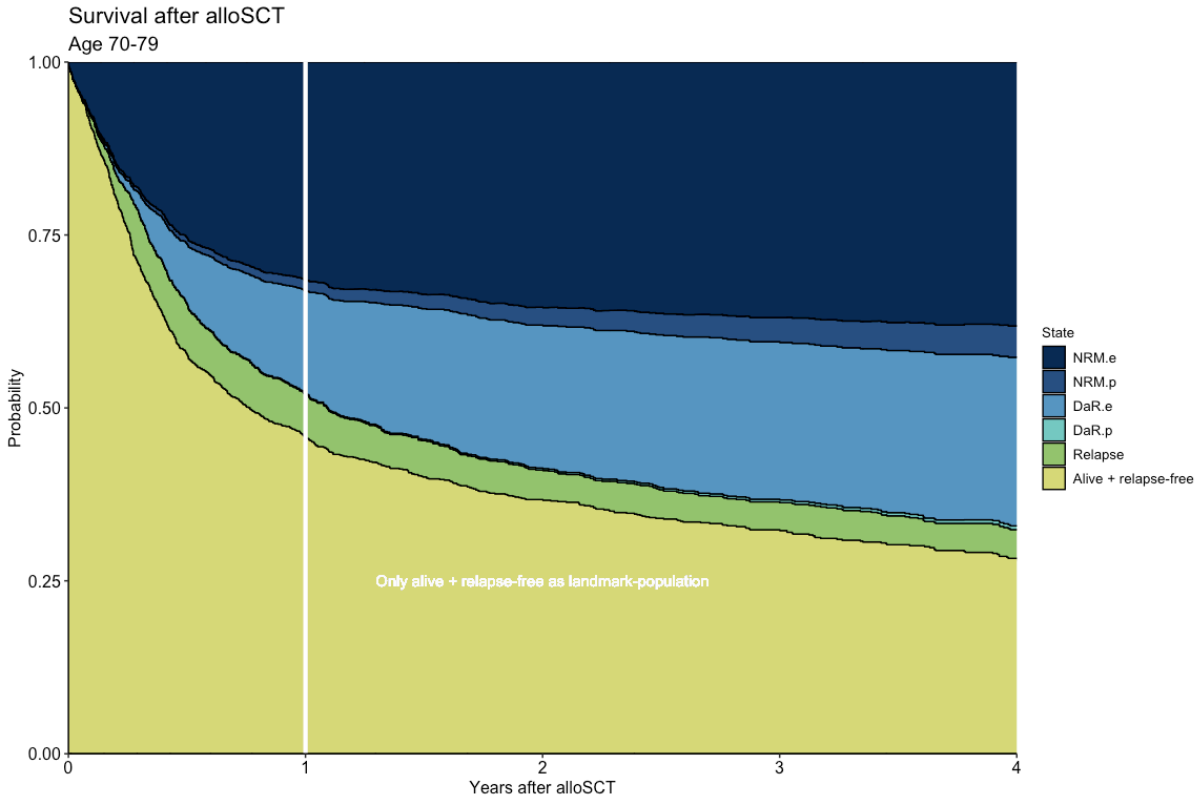


Supplemental figure 4.2. mortality lambda in comparison to German general population (age-, sex- and year-matched) after one year of survival. Epanechnikov kernel smoothing was obtained via relsurv package in R. *Refer to:* https://rdrr.io/cran/relsurv/

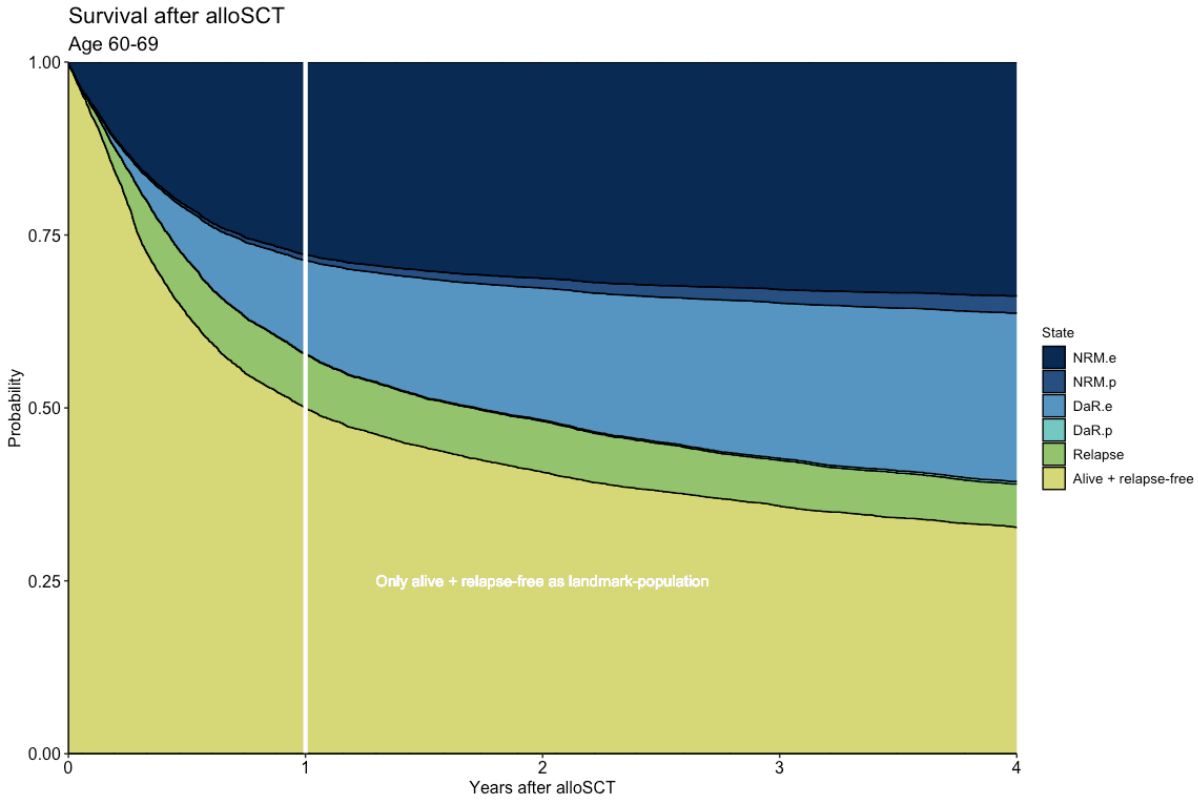


Multistate Estimations in RFS- and GRFS-environments

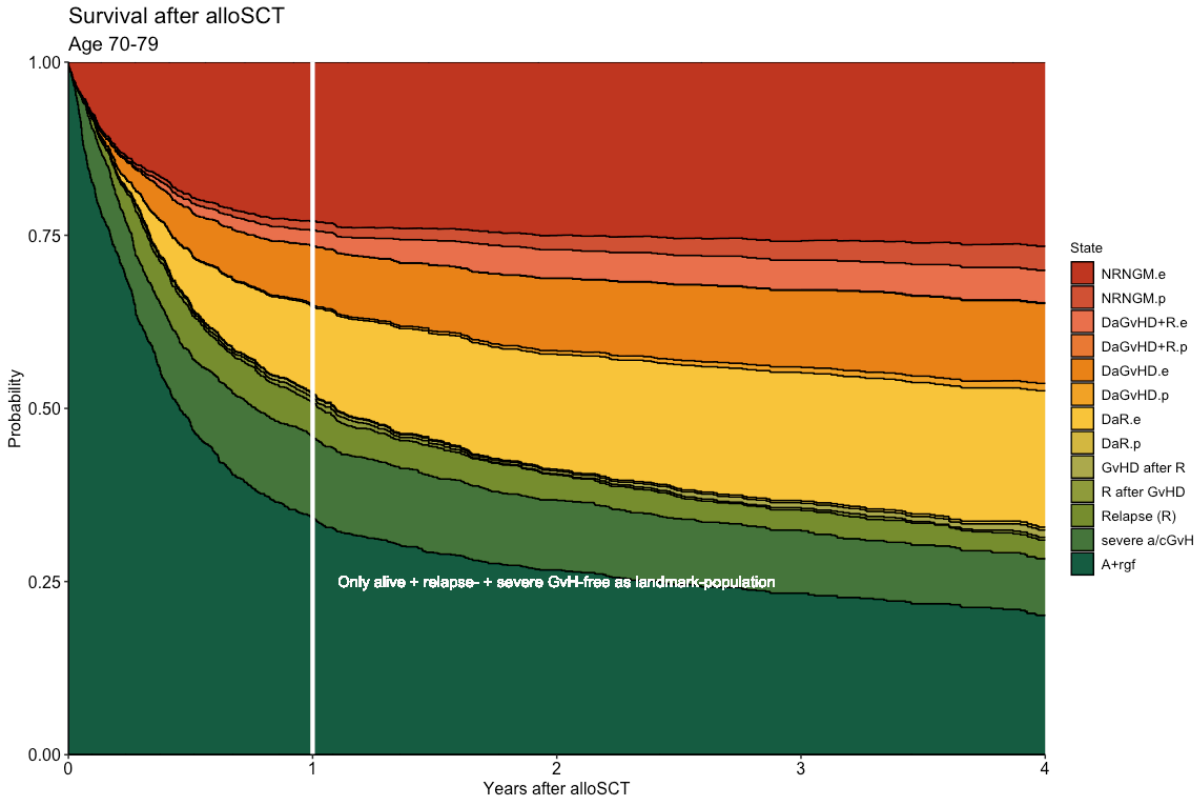
Supplemental figure 5.1 Multistate estimations of relapse-free survival and mortality after alloHSCT for all patients aged 70-79.
NRM.p Non-relapse-mortality DAR Death after relapse NRNGM Non-relapse-non-GvH-mortality DaGvHD+R Death after GvHD and Relapse DaGvHD Death after GvHD R Relapse; .p due to population mortality, .e due to excess mortality



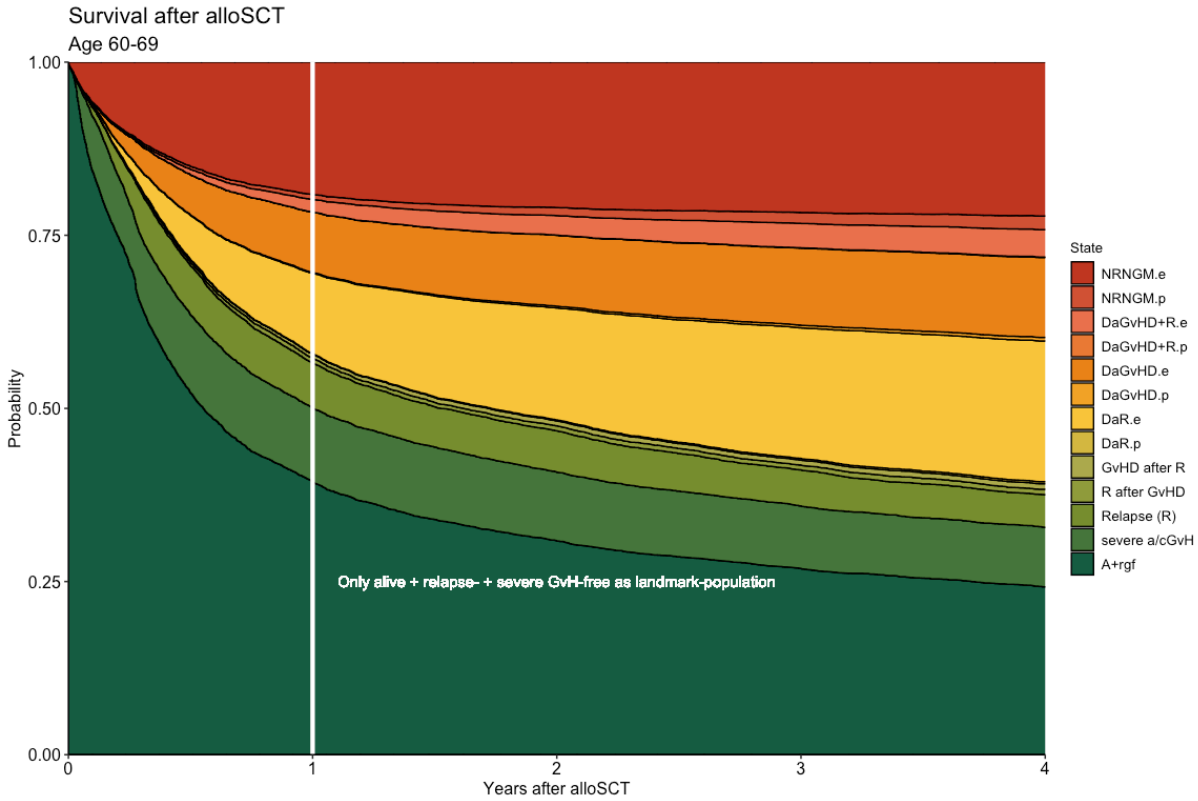
Supplemental figure 5.2. Multistate Estimations of relapse-free survival and mortality after alloHSCT for all patients 60-69.
NRM.p Non-relapse-mortality DAR Death after relapse NRNGM Non-relapse-non-GvH-mortality DaGvHD+R Death after GvHD and Relapse DaGvHD Death after GvHD R Relapse; .p due to population mortality, .e due to excess mortality



Supplemental figure 5.3. Multistate Estimations of GvH-relapse-free survival and mortality after alloHSCT for all patients 70-79.
NRM.p Non-relapse-mortality DAR Death after relapse NRNGM Non-relapse-non-GvH-mortality DaGvHD+R Death after GvHD and Relapse DaGvHD Death after GvHD R Relapse; .p due to population mortality, .e due to excess mortality



Supplemental figure 5.4. Multistate Estimations of GvH-relapse-free survival and mortality after alloHSCT for all patients 60-69.
NRM.p Non-relapse-mortality DAR Death after relapse NRNGM Non-relapse-non-GvH-mortality DaGvHD+R Death after GvHD and Relapse DaGvHD Death after GvHD R Relapse; .p due to population mortality, .e due to excess mortality



Outcomes from RFS-multistate

Supplemental table 3.1. Multistate estimations, patients divided by age group.
All estimations in % [SE] [95CI].

Multistate probabilities of being in state x	**1 year after HSCT, 70+**	**2 years after HSCT, 70+**	**4 years after HSCT, 70+**	**1 year after HSCT, 60-69**	**2 years after HSCT, 60-69**	**4 years after HSCT, 60-69**
alive+relapse-free	45.59% [SE 1.22] [CI 43.26-48.05]	36.75% [SE 0.95] [CI 34.93-38.67]	28.25% [SE 0.87] [CI 26.6-30.01]	49.91% [SE 0.3] [CI 49.32-50.51]	40.7% [SE 0.7] [CI 39.36-42.09]	32.73% [SE 0.67] [CI 31.45-34.06]
alive after or alive with relapse	6.3% [SE 1.15] [CI 4.41-9.01]	4.29% [SE 0.63] [CI 3.23-5.71]	4.15% [SE 0.56] [CI 3.19-5.41]	7.84% [SE 0.33] [CI 7.23-8.51]	7.37% [SE 0.22] [CI 6.96-7.81]	6.28% [SE 0.28] [CI 5.76-6.85]
death after relapse,due to pop.mort	0.13% [SE 0.01] [CI 0.11-0.16]	0.27% [SE 0.03] [CI 0.21-0.34]	0.54% [SE 0.05] [CI 0.46-0.64]	0.08% [SE 0] [CI 0.07-0.08]	0.18% [SE 0] [CI 0.17-0.18]	0.37% [SE 0.01] [CI 0.35-0.39]
death after relapse, due to exc.mort	14.84% [SE 0.96] [CI 13.07-16.85]	20.67% [SE 0.97] [CI 18.86-22.65]	24.37% [SE 1.05] [CI 22.39-26.52]	13.49% [SE 0.2] [CI 13.11-13.88]	19.05% [SE 0.16] [CI 18.73-19.37]	24.33% [SE 0.35] [CI 23.64-25.03]
NRM, pop.mort	1.54% [SE 0.02] [CI 1.51-1.58]	2.58% [SE 0.06] [CI 2.47-2.7]	4.54% [SE 0.11] [CI 4.33-4.76]	0.83% [SE 0.01] [CI 0.82-0.85]	1.42% [SE 0.02] [CI 1.39-1.45]	2.48% [SE 0.04] [CI 2.41-2.55]
NRM, exc.mort	31.59% [SE 1.1] [CI 29.51-33.82]	35.44% [SE 0.96] [CI 33.61-37.36]	38.14% [SE 1.36] [CI 35.57-40.91]	27.84% [SE 0.46] [CI 26.96-28.76]	31.28% [SE 0.58] [CI 30.16-32.44]	33.81% [SE 0.67] [CI 32.51-35.16]

Supplemental table 3.2. Multistate estimations after one year EF-survival, patients divided by age group. All estimations in % [SE] [95CI].

Multistate probabilities of being in state x	**1 year after 1-year-RFS-LM, 70+**	**3 years after 1-year-RFS-LM, 70+**	**1 year after 1-year-RFS-LM, 60-69**	**3 years after 1-year-RFS-LM, 60-69**
alive+relapse-free	80.62% [SE 1.16] [CI 78.36-82.93]	61.97% [SE 1.61] [CI 58.89-65.22]	81.55% [SE 1.11] [CI 79.41-83.75]	65.57% [SE 0.95] [CI 63.74-67.47]
alive after or alive with relapse	4.95% [SE 0.76] [CI 3.67-6.68]	7.39% [SE 1.08] [CI 5.55-9.85]	7.47% [SE 0.48] [CI 6.58-8.48]	9.34% [SE 0.44] [CI 8.52-10.24]

Multistate probabilities of being in state x	1 year after 1-year-RFS-LM, 70+	3 years after 1-year-RFS-LM, 70+	1 year after 1-year-RFS-LM, 60-69	3 years after 1-year-RFS-LM, 60-69
death after relapse,due to pop.mort	0.11% [SE 0.01] [CI 0.08-0.14]	0.53% [SE 0.07] [CI 0.41-0.68]	0.06% [SE 0.01] [CI 0.05-0.07]	0.31% [SE 0.02] [CI 0.28-0.36]
death after relapse, due to exc.mort	3.61% [SE 0.58] [CI 2.63-4.95]	9.16% [SE 1.13] [CI 7.19-11.67]	2.87% [SE 0.2] [CI 2.5-3.28]	9.52% [SE 0.43] [CI 8.72-10.39]
NRM, pop.mort	2.28% [SE 0.05] [CI 2.18-2.39]	6.57% [SE 0.12] [CI 6.35-6.8]	1.18% [SE 0.01] [CI 1.15-1.21]	3.3% [SE 0.05] [CI 3.21-3.4]
NRM, exc.mort	8.44% [SE 0.58] [CI 7.37-9.65]	14.38% [SE 1.52] [CI 11.69-17.68]	6.88% [SE 0.57] [CI 5.85-8.09]	11.95% [SE 0.55] [CI 10.91-13.08]

Outcomes from GRFS-multistate

Supplemental table 3.3. Multistate estimations, patients divided by age group.
All estimations in % [SE] [95CI].

Multistate probabilities of being in state x	1 year after HSCT, 70+	2 years after HSCT, 70+	4 years after HSCT, 70+	1 year after HSCT, 60-69	2 years after HSCT, 60-69	4 years after HSCT, 60-69
alive+GvHD&relapse-free	34.08% [SE 0.95] [CI 32.27-36]	26.69% [SE 0.97] [CI 24.86-28.66]	20.13% [SE 0.63] [CI 18.93-21.42]	39.37% [SE 0.49] [CI 38.41-40.34]	30.87% [SE 0.69] [CI 29.55-32.26]	24.23% [SE 0.56] [CI 23.15-25.35]
alive after or alive with sev. GvHD	11.59% [SE 0.43] [CI 10.78-12.45]	10.12% [SE 0.33] [CI 9.5-10.78]	8.18% [SE 0.57] [CI 7.14-9.37]	10.65% [SE 0.28] [CI 10.12-11.21]	9.93% [SE 0.17] [CI 9.59-10.27]	8.59% [SE 0.28] [CI 8.07-9.15]
alive after or alive with relapse	5.02% [SE 1.02] [CI 3.37-7.48]	3.66% [SE 0.67] [CI 2.55-5.24]	2.68% [SE 0.56] [CI 1.79-4.02]	6.57% [SE 0.41] [CI 5.82-7.42]	5.97% [SE 0.27] [CI 5.46-6.52]	4.73% [SE 0.24] [CI 4.28-5.23]
Relapse after GvHD	0.72% [SE 0.17] [CI 0.45-1.15]	0.13% [SE 0.05] [CI 0.06-0.29]	0.4% [SE 0.11] [CI 0.23-0.71]	0.69% [SE 0.08] [CI 0.56-0.87]	0.71% [SE 0.09] [CI 0.56-0.9]	0.78% [SE 0.06] [CI 0.67-0.91]
GvHD after Relapse	0.56% [SE 0.16] [CI 0.31-1]	0.42% [SE 0.17] [CI 0.19-0.93]	1.05% [SE 0.38] [CI 0.52-2.13]	0.57% [SE 0.03] [CI 0.51-0.64]	0.71% [SE 0.13] [CI 0.51-1.01]	0.79% [SE 0.1] [CI 0.62-1.02]
death after relapse,due to pop.mort	0.11% [SE 0.01] [CI 0.09-0.14]	0.23% [SE 0.03] [CI 0.17-0.29]	0.42% [SE 0.04] [CI 0.35-0.51]	0.07% [SE 0] [CI 0.06-0.07]	0.15% [SE 0] [CI 0.14-0.15]	0.3% [SE 0.01] [CI 0.28-0.31]
death after relapse, due to exc.mort	12.56% [SE 0.94] [CI 10.84-14.55]	16.61% [SE 0.91] [CI 14.92-18.49]	19.68% [SE 1.15] [CI 17.56-22.05]	11.59% [SE 0.16] [CI 11.28-11.9]	16.16% [SE 0.08] [CI 16.01-16.31]	20.32% [SE 0.36] [CI 19.63-21.03]
death after GvHD,due to pop.mort	0.24% [SE 0] [CI 0.23-0.25]	0.52% [SE 0.02] [CI 0.49-0.56]	1.07% [SE 0.04] [CI 0.98-1.16]	0.12% [SE 0] [CI 0.12-0.13]	0.26% [SE 0] [CI 0.25-0.26]	0.52% [SE 0.01] [CI 0.5-0.53]
death after GvHD, due to exc.mort	8.62% [SE 0.44] [CI 7.79-9.53]	10.4% [SE 0.53] [CI 9.41-11.5]	11.54% [SE 0.5] [CI 10.61-12.56]	8.72% [SE 0.22] [CI 8.31-9.16]	10.24% [SE 0.28] [CI 9.71-10.8]	11.53% [SE 0.36] [CI 10.84-12.26]
death after relapse+GvHD,due to pop.mort	0.02% [SE 0] [CI 0.02-0.02]	0.04% [SE 0] [CI 0.03-0.05]	0.11% [SE 0.02] [CI 0.08-0.17]	0.01% [SE 0] [CI 0.01-0.01]	0.03% [SE 0] [CI 0.02-0.03]	0.07% [SE 0.01] [CI 0.06-0.09]
death after relapse+GvHD, due to exc.mort	2.23% [SE 0.18] [CI 1.9-2.62]	4.1% [SE 0.17] [CI 3.78-4.43]	4.68% [SE 0.24] [CI 4.23-5.17]	1.83% [SE 0.07] [CI 1.71-1.96]	2.81% [SE 0.15] [CI 2.53-3.11]	3.95% [SE 0.18] [CI 3.62-4.32]

Multistate probabilities of being in state x	1 year after HSCT, 70+	2 years after HSCT, 70+	4 years after HSCT, 70+	1 year after HSCT, 60-69	2 years after HSCT, 60-69	4 years after HSCT, 60-69
NRNGM, pop.mort	1.3% [SE 0.02] [CI 1.27-1.34]	2.06% [SE 0.05] [CI 1.98-2.15]	3.48% [SE 0.1] [CI 3.28-3.69]	0.71% [SE 0.01] [CI 0.69-0.73]	1.17% [SE 0.02] [CI 1.13-1.2]	1.97% [SE 0.04] [CI 1.9-2.04]
NRNGM, exc.mort	22.95% [SE 0.95] [CI 21.16-24.89]	25.02% [SE 1] [CI 23.13-27.07]	26.58% [SE 1.15] [CI 24.42-28.93]	19.1% [SE 0.27] [CI 18.57-19.64]	21% [SE 0.33] [CI 20.36-21.66]	22.22% [SE 0.31] [CI 21.61-22.84]

Supplemental table 3.4. Multistate estimations after one year of GRF-survival, patients divided by age group.
All estimations in % [SE] [95CI]. GRFS Graft-versus-Host-free-relapse-free-survival.

Multistate probabilities of being in state x	1 year after 1-year-GRFS-LM, 70+	3 years after 1-year-GRFS-LM, 70+	1 year after 1-year-GRFS-LM, 60-69	3 years after 1-year-GRFS-LM, 60-69
alive+GvHD&relapse-free	78.31% [SE 2.78] [CI 73.05-83.96]	59.07% [SE 1.73] [CI 55.77-62.57]	78.43% [SE 0.87] [CI 76.73-80.16]	61.54% [SE 0.9] [CI 59.79-63.34]
alive after or alive with sev. GvHD	3.72% [SE 0.96] [CI 2.24-6.18]	4.27% [SE 0.88] [CI 2.85-6.4]	3.94% [SE 0.37] [CI 3.27-4.74]	5.49% [SE 0.49] [CI 4.61-6.54]
alive after or alive with relapse	5.5% [SE 1.27] [CI 3.49-8.66]	6.42% [SE 1.28] [CI 4.34-9.49]	7.77% [SE 0.57] [CI 6.73-8.97]	9.03% [SE 0.56] [CI 8-10.19]
Relapse after GvHD	0.02% [SE 0.01] [CI 0.01-0.04]	0.18% [SE 0.06] [CI 0.1-0.35]	0.15% [SE 0.02] [CI 0.11-0.18]	0.34% [SE 0.06] [CI 0.24-0.48]
GvHD after Relapse	0.25% [SE 0.21] [CI 0.04-1.36]	1.64% [SE 0.8] [CI 0.63-4.29]	0.16% [SE 0.08] [CI 0.06-0.4]	0.69% [SE 0.13] [CI 0.48-1]
death after relapse,due to pop.mort	0.11% [SE 0.02] [CI 0.08-0.17]	0.51% [SE 0.08] [CI 0.38-0.69]	0.06% [SE 0.01] [CI 0.05-0.07]	0.31% [SE 0.02] [CI 0.27-0.36]
death after relapse, due to exc.mort	3.1% [SE 0.75] [CI 1.92-4.99]	9.13% [SE 1.26] [CI 6.97-11.96]	3.05% [SE 0.22] [CI 2.65-3.51]	9.74% [SE 0.39] [CI 9.02-10.53]
death after GvHD,due to pop.mort	0.07% [SE 0.02] [CI 0.04-0.11]	0.31% [SE 0.07] [CI 0.2-0.48]	0.03% [SE 0] [CI 0.03-0.04]	0.17% [SE 0.02] [CI 0.14-0.21]
death after GvHD, due to exc.mort	0.45% [SE 0.15] [CI 0.24-0.86]	0.95% [SE 0.35] [CI 0.46-1.95]	0.35% [SE 0.07] [CI 0.24-0.5]	1.01% [SE 0.07] [CI 0.87-1.16]

Multistate probabilities of being in state x	1 year after 1-year-GRFS-LM, 70+	3 years after 1-year-GRFS-LM, 70+	1 year after 1-year-GRFS-LM, 60-69	3 years after 1-year-GRFS-LM, 60-69
death after relapse+GvHD,due to pop.mort	0% [SE 0] [CI 0-0.01]	0.07% [SE 0.02] [CI 0.03-0.13]	0% [SE 0] [CI 0-0]	0.02% [SE 0] [CI 0.02-0.03]
death after relapse+GvHD, due to exc.mort	0.15% [SE 0.05] [CI 0.08-0.27]	0.42% [SE 0.2] [CI 0.16-1.09]	0.07% [SE 0.02] [CI 0.04-0.13]	0.52% [SE 0.06] [CI 0.43-0.65]
NRNGM, pop.mort	2.23% [SE 0.06] [CI 2.12-2.34]	6.38% [SE 0.23] [CI 5.95-6.85]	1.15% [SE 0.01] [CI 1.14-1.17]	3.2% [SE 0.04] [CI 3.13-3.27]
NRNGM, exc.mort	6.08% [SE 0.37] [CI 5.39-6.86]	10.64% [SE 2.07] [CI 7.27-15.59]	4.84% [SE 0.32] [CI 4.25-5.51]	7.93% [SE 0.36] [CI 7.26-8.66]

2. Completeness of Follow-up

To provide an appropriate estimation of survival rates, we broke follow-up down to observed and potential periods to enable calculation of completeness of follow-up (Clark TG, Altman DG, De Stavola BL. Quantification of the completeness of follow-up. Lancet. 2002).

Criteria for completeness were: (1) death (2) last FU < 1 year before data set closure (3) FU > 10 years. Only patients with transplantation two years before dataset closure were part of the statistical analysis. Median observed follow-up (documented follow-up irrespective of censor or death) was 1 year [range 0-22.4] and median potential follow-up was 1.8 years [range 0-10] for all patients. Potential follow-up for a patient with death at last date of follow-up was his survival time while in all censored patients the potential follow-up was the period between transplantation and 2020-05-01. Dataset closure was 2021-05-01. Completeness was the ratio of the sum of all observed follow-up and the sum of all potential follow-up times 100 (Clark TG, Altman DG, De Stavola BL. Quantification of the completeness of follow-up. Lancet. 2002).

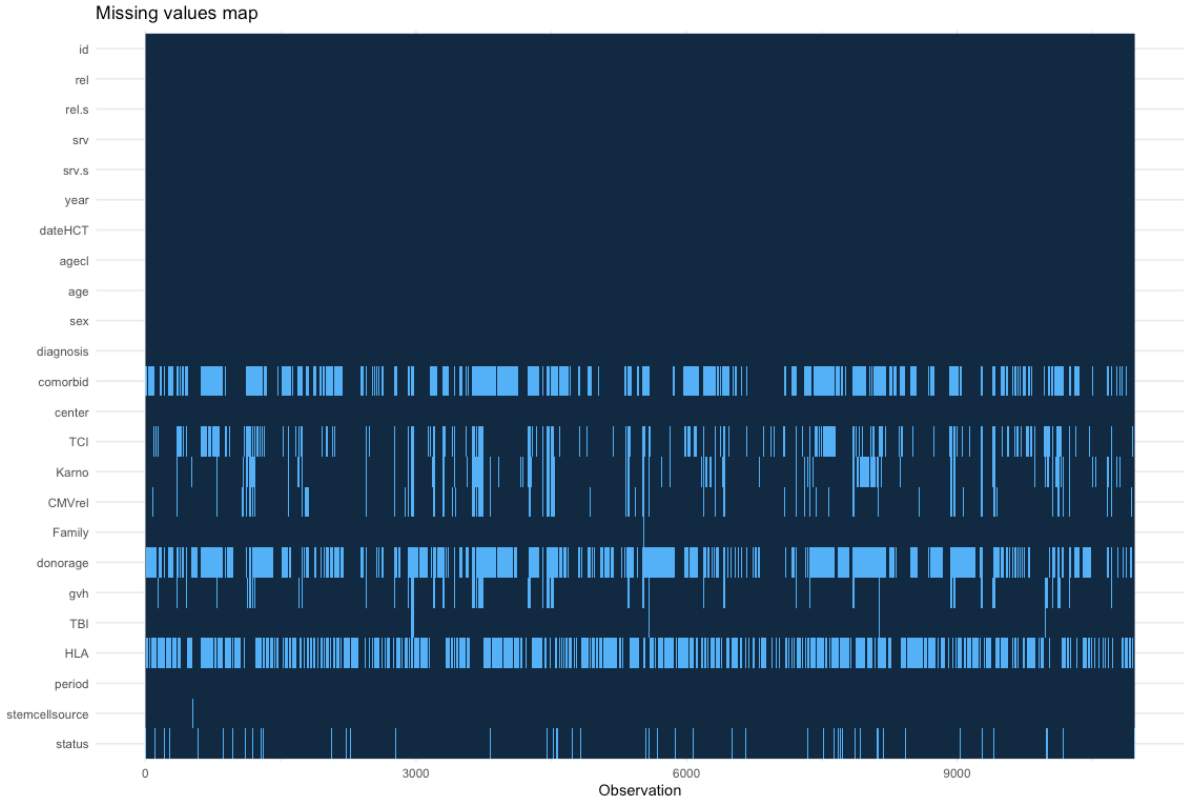
Completeness (C-Index) was 60% averaged over patients. Completeness of follow-up as a potential source of bias between age groups was examined and found similar (60-69: 60%, 70-79: 60.6%).

The final analysis cohort for all models (Kaplan-Meier, Multistate, Regression) was built from all centers achieving a 50% completeness of follow-up (50 centers, n = 8,560 60-69, n = 1,427 70-79). Within the analysis cohort, observed follow-up was 1 year [range 0-22.4] and potential follow-up was 1.8 years [range 0-22.2] for all patients. Completeness (C-Index) was 64.1%, again averaged over patients.

3. **Approach to missingness**

1. *Amount of missing data:* What is the number of missing values for each variable of interest? What is the number of cases with complete data for the analyses of interest?

   1.1. In covariates for multivariable analysis roughly 10% of data was missing. The highest proportions were observed for donor data (donor age, HLA-data) and comorbidity. For missing event data in relapse, aGvHD and cGvHD please refer below (7.3-7.5).



Graphical overview of missing values before imputation. Light blue depicts missing values. Dark blue data was fully available after <1% of patients was excluded for violation of inclusion criteria. On average 8.88% of data was missing, which was answered with imputation of 100 dataframes and 10 iterations. Top three missing data were HLA data (56.98%), Donor Age (52.25%) and Comorbidity (45.2%).

GVHD prophy – GvHD Prophylaxis, Status – Remission status at HSCT (CR vs. no CR only)

2. Reasons for missingness

   2.1. The reasons for missingness remain unclear. Some lack of full documentation might be linked to early death – spoken from our experience. Although some clustering could be observed, most of the missing data did not follow an obvious pattern (see graphical display). The only exception might be a known underreport of HLA data in unrelated donors. We nevertheless have to assume a center dependent degree of missingness for some covariates (donor age, comorbidities, HLA-match). In sum we assumed a missing at random (MAR) pattern for missing values.

3. Consequences We suppose the consequences to be minimal for most of the article's content. Primary outcomes as death date and status as well as relapse date and status are fully reported. Some important covariates however (donor age, HLA-data, comorbidities) show a high proportion of missingness (> 40%) with introducing possible bias into regression analyses. However, the main covariates of interest (age) were fully reported. Sex and year of HSCT were also nearly fully reported which would introduce minimal bias to relative survival analysis.

4. Methods of imputation: A multiple imputation strategy was used to account for the high proportion of missingness. We chose a higher count of imputed datasets to be accountable for the higher proportion of missing covariate data in some covariates (m=100, iterations = 10, m = 20, iterations = 10 for additive model).

   Missing time to aGvHD was simply filled with random day counts from all reported patients.

5. Software: We used R and its package mice to obtain multiple datasets that could be introduced into regression analyses thereafter. The linked method there was **multiple imputation by chained equations** after Stef van Buuren and Karin Groothuis-Oudshoorn, 2011. (Ref.: van Buuren, S., & Groothuis-Oudshoorn, K. (2011). mice: Multivariate Imputation by Chained Equations in R. Journal of Statistical Software, 45(3), 1–67. https://doi.org/10.18637/jss.v045.i03)
6. Number of imputed datasets: m = 100, max interations 10 for Cox regression, 20 for additive model due to computational limits.
7. Imputation model:
   7.1. An imputation model was set after creating a predictor matrix. At least 30% of a predictor's values had to be available to be considered a predictor. A minimum correlation of 0.1 (Pearson's r) was set to choose possible predictors for every imputed variable. Thereby, we aimed to prevent massive imputation.

   All covariates with exception to survival data were used for imputation. A Nelson-Aalen estimate and the survival status indicator of the cumulative hazard for overall survival was integrated. Categorical covariates with two possible values were imputed using logistic regression and covariates with more than two outcomes after Bayesian polytomous regression modelling ("logreg," "polyreg", see https://www.rdocumentation.org/packages/mice/versions/3.14.0/topics/mice.impute.polyreg). Numeric values were imputed after predictive mean matching ("pmm").

   7.2. Relapse, aGvHD and cGvHD were treated as "*non-existing/no event"* when reported as not available (NA).

   7.3. Missing data (NA) accounted for 462/9987 patients concerning relapse.

7.4. 6734/9987 patients concerning cGvHD were documented “NA” and were treated as non-sufferers. This is how it is supposed to be documented correct in the registry. Stating this, we believe in and fully accept an error of 5%.

Concerning the first entries for cGvHD exemplarily, 1326/9987 patients were documented as suffering from extensive GvHD. Other entries (“ “, “moderate”, “99”, “NA”) were documented as not relevant to the study. In the end, 1614 patients (respecting all possible entry and grade data) could be registered with severe cGvHD and a documented date.

7.5. 539 (NA) + 68 (present, grade unknown)/9987 for acute GvHD were unknown and treated as “no acute GvHD” until day 100. Of all 9987, 1198 had aGvHD grade 3 (n=785) or grade 4 (n=413). In addition, for nearly half of these (n=587) the date of symptom onset was missing. This was filled with random data from all other entered aGvHD dates with respect to the overall survival of the respected patient. In the end, date data were fully completed in this random method, using a “seed” for reproducibility. Median and mean days to aGvHD were 25 days and 37 days for all grade 3+4 before random fill up and 24 and 35 thereafter.

8. Derived variables:

8.1. Some data was imputed in its processed format (CMV relation). We preferred an imputation for categorical values. Donor age however was kept in its numerical form and was mutated into its factor (“younger than median”, “older than median”) in a second step in all imputed datasets.

9. Diagnostics: In multiple imputation it is of crucial importance to introduce variance in the imputed values between all imputations. It is therefore important that imputed values graphically show convergence (crossing lines between imputations) without creating a trend value (low variance).

9.1. The success of iterations could be observed observing a convergence of mean and sd in most of the covariates. HLA-data, comorbidities and donor age however were difficult to be imputed. After imputation, all data was plausible with the exception for HLA-data where unmatched donors seemed to be quantitively overestimated.

9.2. Convergence was checked graphically (see below).

10. Pooling: The results of regression analyses were pooled (R package mice, pool(); Rubin's Rule; see Rubin, D.B. (1987). Multiple Imputation for Nonresponse in Surveys. New York: John Wiley and Sons.) for all datasets and displayed. No transformation was undergone.

11. Complete-case analysis: A complete case-analysis (n=1153) was done for the chosen covariates for the overall survival Cox regression. The results for the main covariate of interest (age group) was similar.

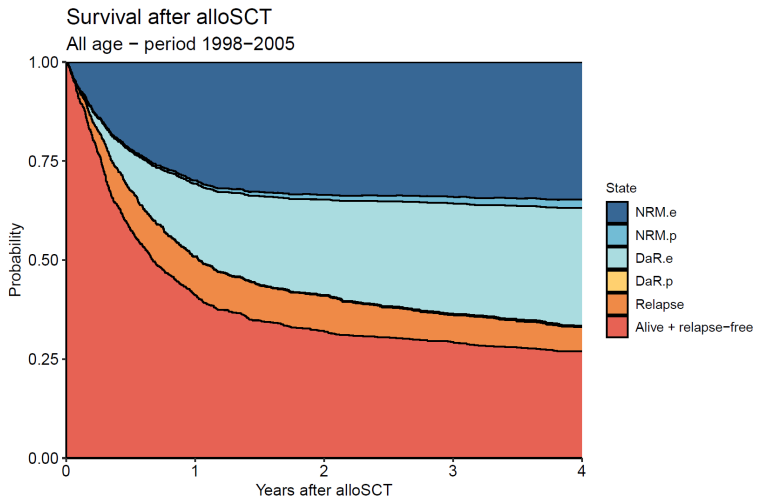
term	string
Age 70-79, ref. 60-69	HR 1.32 [1.1-1.59], p=0.003
CLL, ref. AML	HR 1.11 [0.58-2.13], p=n.s
CML	HR 1.24 [0.51-3.03], p=n.s
Lymphoma	HR 1.16 [0.79-1.69], p=n.s
MDS/MPN	HR 0.7 [0.59-0.84], p=<0.001
Others	HR 0.95 [0.6-1.49], p=n.s
Plasma cell disorders	HR 1.43 [0.85-2.38], p=n.s

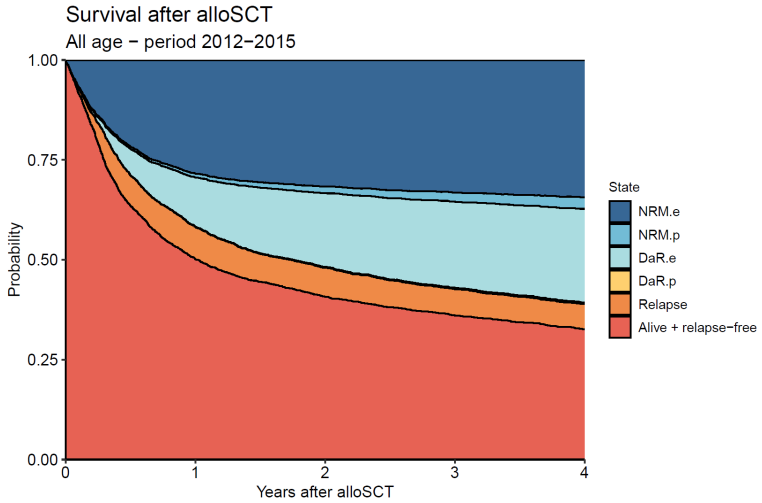
term	string
Male, ref. female	HR 1.04 [0.89-1.21], p=n.s
Comorbidity, ref. No	HR 1.12 [0.95-1.31], p=n.s
Int TCI, ref. high	HR 0.96 [0.52-1.77], p=n.s
Low TCI	HR 0.99 [0.53-1.82], p=n.s
Karnofsky < 80, ref. 90-100	HR 1.78 [1.43-2.22], p=<0.001
Karnofsky 80	HR 1.12 [0.95-1.32], p=n.s
CMV – both positive, ref. both negative	HR 1.21 [1.01-1.45], p=0.037
CMV – neg. patient, pos. donor	HR 1.17 [0.88-1.56], p=n.s
CMV – pos. patient, neg. donor	HR 1.08 [0.87-1.33], p=n.s
Unrelated, ref. related	HR 1.02 [0.81-1.29], p=n.s
TBI, ref. no	HR 1.18 [0.95-1.46], p=n.s
HLA, ref. match	HR 1.34 [1.05-1.7], p=0.02
Donor Age	HR 1.01 [1-1.01], p=n.s
Period 2009-2018, ref. 1998-2008	HR 1.06 [0.85-1.31], p=n.s
Stemcellsource, ref. BM	HR 0.81 [0.61-1.08], p=n.s
Status in CR, ref. No	HR 0.69 [0.57-0.83], p=<0.001

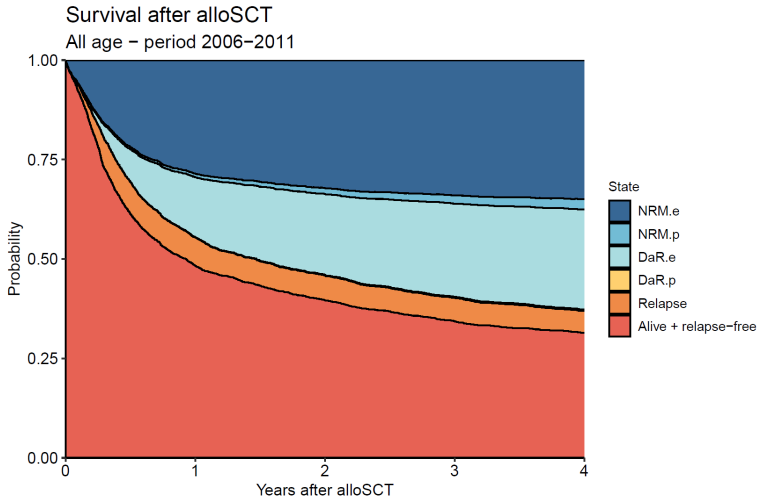
Supplemental table 4. Hazard ratios, derived from complete case analysis before imputation (n = 1453).

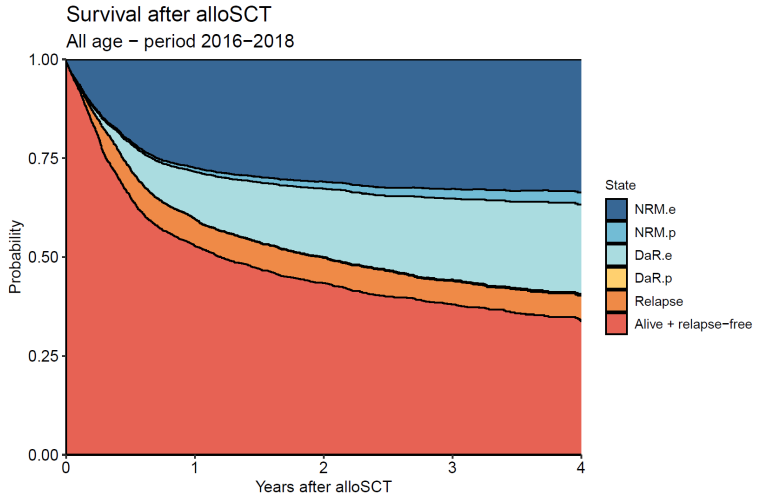
4. Additional data

Supplemental figure 6

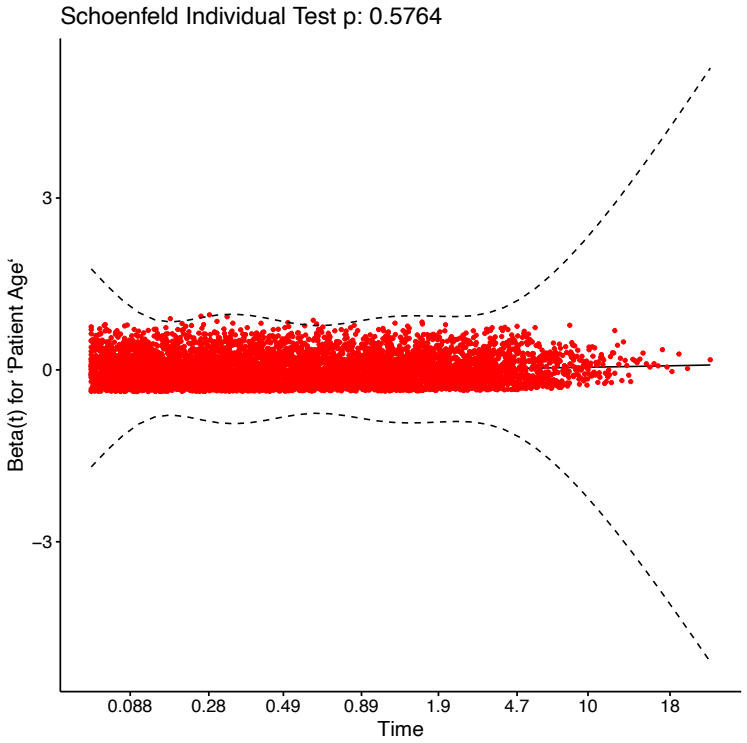




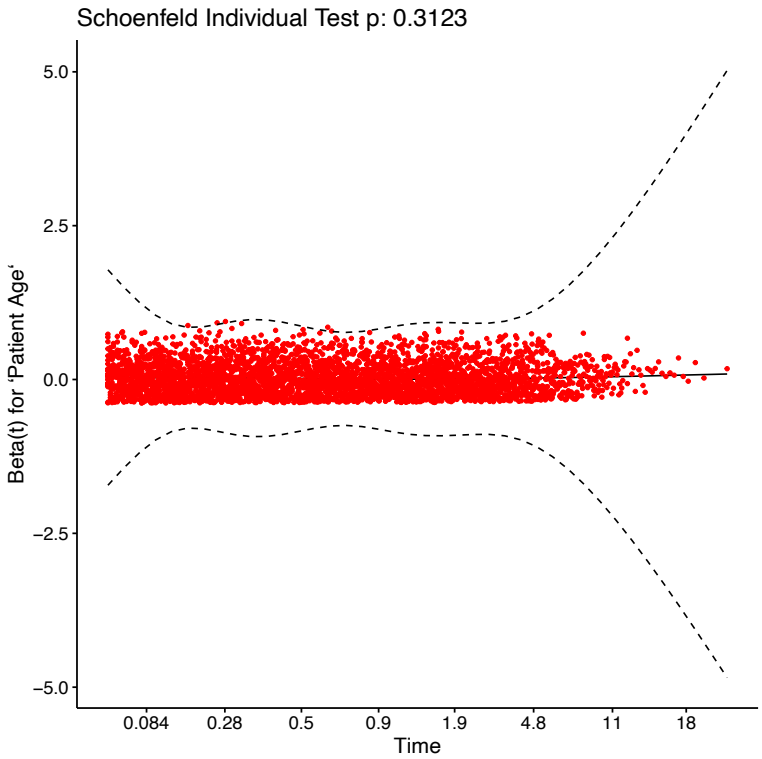




Supplemental figure 7.1 – Schoenfeld residuals for follow-up > 50%



Supplemental figure 7.2 – Schoenfeld residuals for follow-up > 80%



	Cox regression regarding overall survival (OS)			Additive proportional hazards model regarding excess mortality[+]		
Covariate	**Total FU*** **HR [95%CI]**	**First year of FU*** **HR [95%CI]**	**Years 1+ of FU*** **HR [95%CI]**	**Total FU*** **HR [95%CI]**	**First year of FU*** **HR [95%CI]**	**Years 1+ of FU*** **HR [95%CI]**
Age group **ref. 60-69**	1	1	1	1	1	1
70-79	1.19 [1.1-1.28], p<0.001	1.18 [1.08-1.29], p<0.001	1.22 [1.07-1.4], p=0.004	1.14 [1.05-1.24], p=0.001	1.16 [1.06-1.27], p=0.001	1.09 [0.91-1.3], p=0.35
Disease, **ref. acute leukemia**	1	1	1	1	1	1
CLL	0.58 [0.49-0.68], p<0.001	0.53 [0.43-0.65], p<0.001	0.68 [0.53-0.88], p=0.003	0.53 [0.44-0.63], p<0.001	0.5 [0.41-0.62], p<0.001	0.62 [0.44-0.87], p=0.006
CML	0.73 [0.59-0.9], p=0.003	0.78 [0.6-1], p=0.048	0.65 [0.45-0.94], p=0.021	0.72 [0.56-0.91], p=0.006	0.77 [0.59-1], p=0.05	0.54 [0.31-0.94], p=0.028
Lymphoma	R 1.08 [0.97-1.19], p=0.16	1.19 [1.06-1.33], p=0.004	0.83 [0.68-1.02], p=0.08	1.1 [0.99-1.23], p=0.09	1.19 [1.06-1.34], p=0.004	0.79 [0.61-1.04], p=0.09
MDS/MPN	0.76 [0.71-0.81], p<0.001	0.75 [0.69-0.81], p<0.001	0.78 [0.69-0.89], p<0.001	0.74 [0.68-0.8], p<0.001	0.73 [0.67-0.8], p<0.001	0.76 [0.65-0.9], p=0.001
Plasma cell disorders	0.97 [0.86-1.09], p=0.56	0.81 [0.7-0.94], p=0.007	1.29 [1.07-1.55], p=0.007	0.87 [0.76-0.99], p=0.036	0.8 [0.69-0.94], p=0.006	1.07 [0.84-1.37], p=0.59
Others	1.06 [0.92-1.22], p=0.42	1.02 [0.86-1.22], p=0.78	1.15 [0.89-1.49], p=0.28	1.06 [0.91-1.23], p=0.47	1.03 [0.86-1.22], p=0.77	1.18 [0.87-1.61], p=0.3
P-value after Cox Anova	< 0.001	< 0.001	< 0.001			
Sex ref. female	1	1	1	1	1	1
male	1.08 [1.03-1.14], p=0.004	1.05 [0.98-1.12], p=0.17	1.16 [1.05-1.27], p=0.003	1.06 [1-1.12], p=0.06	1.04 [0.97-1.11], p=0.23	1.11 [0.98-1.25], p=0.1

	Cox regression regarding overall survival (OS)			Additive proportional hazards model regarding excess mortality+		
Covariate	**Total FU*** **HR [95%CI]**	**First year of FU*** **HR [95%CI]**	**Years 1+ of FU*** **HR [95%CI]**	**Total FU*** **HR [95%CI]**	**First year of FU*** **HR [95%CI]**	**Years 1+ of FU*** **HR [95%CI]**
Comorbidity- **ref. No**	1	1	1	1	1	1
Yes	1.16 [1.07-1.25], p<0.001	1.18 [1.07-1.29], p<0.001	1.12 [0.99-1.26], p=0.07	1.16 [1.07-1.26], p<0.001	1.2 [1.1-1.31], p<0.001	1.05 [0.89-1.24], p=0.54
TCI, **ref. high**	1	1	1	1	1	1
Intermediate	0.93 [0.77-1.12], p=0.44	0.92 [0.72-1.16], p=0.47	0.95 [0.7-1.31], p=0.77	0.93 [0.68-1.27], p=0.63	0.92 [0.66-1.27], p=0.59	0.97 [0.61-1.54], p=0.89
Low	0.91 [0.75-1.1], p=0.32	0.93 [0.73-1.18], p=0.53	0.87 [0.63-1.21], p=0.41	0.93 [0.68-1.27], p=0.63	0.94 [0.68-1.31], p=0.71	0.89 [0.56-1.39], p=0.59
P-value after Cox Anova	0.55	0.77	0.31			
Karnofsky Pef. Index, **ref. 90-100**	1	1	1	1	1	1
80	1.27 [1.19-1.35], p<0.001	1.31 [1.22-1.42], p<0.001	1.17 [1.04-1.32], p=0.008	1.3 [1.21-1.39], p<0.001	1.33 [1.23-1.44], p<0.001	1.2 [1.01-1.42], p=0.035
<80	1.84 [1.68-2.02], p<0.001	1.96 [1.75-2.18], p<0.001	1.53 [1.27-1.85], p<0.001	1.95 [1.77-2.15], p<0.001	2.04 [1.82-2.3], p<0.001	1.56 [1.24-1.97], p<0.001
P-value after Cox Anova	< 0.001	< 0.001	< 0.001			
CMV relation, **ref. both IgG negative**	1	1	1	1	1	1
Both positive	1.14 [1.07-1.22], p<0.001	1.2 [1.11-1.31], p<0.001	1.03 [0.92-1.16], p=0.59	1.19 [1.1-1.28], p<0.001	1.24 [1.13-1.36], p<0.001	1.04 [0.89-1.21], p=0.65

	Cox regression regarding overall survival (OS)			Additive proportional hazards model regarding excess mortality[+]		
Covariate	**Total FU*** **HR [95%CI]**	**First year of FU*** **HR [95%CI]**	**Years 1+ of FU*** **HR [95%CI]**	**Total FU*** **HR [95%CI]**	**First year of FU*** **HR [95%CI]**	**Years 1+ of FU*** **HR [95%CI]**
Patient neg. donor pos.	1.09 [0.98-1.22], p=0.1	1.12 [0.98-1.29], p=0.09	1.04 [0.86-1.25], p=0.71	1.09 [0.97-1.24], p=0.16	1.12 [0.97-1.29], p=0.14	1.01 [0.8-1.29], p=0.91
Patient pos. donor neg.	1.23 [1.13-1.33], p<0.001	1.31 [1.19-1.43], p<0.001	1.07 [0.93-1.23], p=0.38	1.3 [1.19-1.42], p<0.001	1.35 [1.22-1.5], p<0.001	1.14 [0.96-1.36], p=0.13
P-value after Cox Anova	< 0.001	< 0.001	0.85			
Donor Type, **ref. related**	1	1	1	1	1	1
Unrelated	1.11 [1.03-1.19], p=0.007	1.15 [1.05-1.26], p=0.002	1.04 [0.91-1.18], p=0.58	1.14 [1.04-1.25], p=0.005	1.16 [1.05-1.28], p=0.003	1.07 [0.9-1.27], p=0.44
Donor Type, HLA-match, **ref. match**	1	1	1	1	1	1
Unmatched	1.33 [1.19-1.49], p<0.001	1.38 [1.21-1.57], p<0.001	1.21 [1-1.46], p=0.05	1.37 [1.13-1.67], p=0.007	1.4 [1.13-1.74], p=0.008	1.27 [0.99-1.62], p=0.06
TBI part of conditioning, **ref. No**	1	1	1	1	1	1
Yes	1.14 [1.06-1.22], p<0.001	1.13 [1.03-1.23], p=0.008	1.15 [1.01-1.32], p=0.042	1.14 [1.05-1.23], p=0.001	1.14 [1.04-1.24], p=0.005	1.14 [0.96-1.35], p=0.13
Donor Age, **ref. higher than median**	1	1	1	1	1	1
Lower	0.86 [0.79-0.93], p<0.001	0.86 [0.78-0.95], p=0.004	0.84 [0.73-0.97], p=0.018	0.85 [0.74-0.99], p=0.036	0.86 [0.76-0.99], p=0.036	0.82 [0.64-1.05], p=0.1
Period, **ref. 1998-2008**	1	1	1	1	1	1
2009-2018	0.95 [0.89-1.01], p=0.09	0.9 [0.84-0.97], p=0.009	1.04 [0.93-1.16], p=0.51	0.92 [0.85-0.99], p=0.021	0.9 [0.83-0.97], p=0.008	1 [0.86-1.15], p=0.96

	Cox regression regarding overall survival (OS)			Additive proportional hazards model regarding excess mortality[+]		
Covariate	**Total FU*** **HR [95%CI]**	**First year of FU*** **HR [95%CI]**	**Years 1+ of FU*** **HR [95%CI]**	**Total FU*** **HR [95%CI]**	**First year of FU*** **HR [95%CI]**	**Years 1+ of FU*** **HR [95%CI]**
Stem cell source, **ref. Bone marrow**	1	1	1	1	1	1
Peripheral Blood	0.91 [0.81-1.02], p=0.11	0.95 [0.83-1.09], p=0.45	0.82 [0.68-1], p=0.05	0.92 [0.81-1.05], p=0.23	0.95 [0.82-1.11], p=0.52	0.82 [0.64-1.05], p=0.11
Remission state at HSCT, **ref. no CR**	1	1	1	1	1	1
Complete remission	0.71 [0.66-0.75], p<0.001	0.66 [0.61-0.72], p<0.001	0.82 [0.73-0.92], p<0.001	0.67 [0.63-0.72], p<0.001	0.65 [0.6-0.7], p<0.001	0.76 [0.66-0.88], p<0.001
Follow-up year 0-1, Hazard	NA	NA	NA	0.53 [0.35-0.81], p=0.006	0.49 [0.32-0.76], p=0.	Not evaluated
Follow-up year 1-2, Hazard	NA	NA	NA	0.17 [0.11-0.26], p<0.001	NA	0.23 [0.13-0.4], p<0.001
Follow-up year 2-3, Hazard	NA	NA	NA	0.11 [0.07-0.16], p<0.001	NA	0.14 [0.08-0.25], p<0.001
Follow-up year 3-4, Hazard	NA	NA	NA	0.07 [0.05-0.11], p<0.001	NA	0.09 [0.05-0.17], p<0.001
Likelihood Ratio Test	p<0.001	p < 0.001	p < 0.001	NA	NA	NA

[+] See Appendix for model reference

Supplemental table 5. Regression analyses – full model. Values obtained from a multivariable Cox regression model are depicted overall and separately for the first year and subsequent years of follow-up. Likewise, a Cox model was fitted for excess hazard only. An overall p-value of a likelihood ratio test was added. FU follow up.

5. Addressing possible bias throughout the manuscript – patients transplanted after 2005

Supplemental table 6 - Detailed outcome data – patients transplanted after 2005 and with a center-follow up of 50%, n = 7739

	Overall survival p<0.001⁺		**Relapse-free survival p<0.001⁺**		**Graft-versus-Host-relapse-free survival p<0.001⁺**		**NRM p<0.001***		**Relapse p=0.78***		**Sev. cGvHD p=0.47***		**Sev. aGvHD P=0.96***	
	60-69	**70-79**	**60-69**	**70-79**	**60-69**	**70-79**	**60-69**	**70-79**	**60-69**	**70-79**	**60-69**	**70-79**	**60-69**	**70-79**
Median	1.9 [95CI, 1.7-2.1]	1.1 [1-1.3]	1.1 [1-1.2]	0.8 [0.7-0.9]	0.6 [0.5-0.6]	0.5 [0.4-0.5]								
Day 100													11.4% [10.7-12.2]	11.2% [9.5-13.1]
1 year	58.7% [57.5-60.0]	51.7% [48.9-54.7]	51.2% [49.9-52.4]	45.6% [42.9-48.6]	40.3% [39.1-41.5]	33.8% [31.2-36.6]	28.6% [27.5-29.7]	33.8% [31.2-36.6]	20.2% [19.3-21.3]	20.5% [18.3-22.9]	12.8% [11.9-13.6	14.5% [12.6-16.6]		

	Overall survival p<0.001+		Relapse-free survival p<0.001+		Graft-versus-Host-relapse-free survival p<0.001+		NRM p<0.001*		Relapse p=0.78*		Sev. cGvHD p=0.47*		Sev. aGvHD P=0.96*	
	60-69	**70-79**	**60-69**	**70-79**	**60-69**	**70-79**	**60-69**	**70-79**	**60-69**	**70-79**	**60-69**	**70-79**	**60-69**	**70-79**
2 years	49.1% [47.9-50.4]	41.6% [38.8-44.5]	42.0% [40.8-43.3]	37.2% [34.4-40.1]	31.8% [30.6-33.0]	26.7% [24.3-29.4]	32.6% [31.5-33.8]	38.3% [35.5-41.1]	25.4% [24.3-26.5.]	24.5% [22.1-27.1]	15.1% [14.2-16.0]	16.6% [14.5-18.8]		
3 years	43.4% [42.1-44.7]	36.9% [34.1-39.9]	36.9% [35.7-38.2]	32.9% [30.2-35.8]	27.6% [26.5-28.8]	23.5% [21.1-26.2]	35.0% [33.8-36.2]	40.7% [37.8-43.6]	28.1% [26.9-29.2]	26.4% [23.9-29.0]	16.1% [15.2-17.0]	17.2% [15.0-19.4]		
4 years	39.8% [38.5-41.1]	32.6% [29.8-35.7]	33.6% [32.4-34.9]	28.6% [26.0-31.6]	24.9% [23.7-26.0]	20.1% [17.8-22.8]	36.5% [35.3-37.8]	43.1% [40.1-46.1]	29.8% [28.6-31.0]	28.2% [25.6-31.0]	16.9% [16.0-17.9]	18.0% [15.8-20.3]		
+ logrank, * Gray's test														

Detailed survival data. OS overall survival, RFS relapse-free survival, GRFS Graft-versus-Host-relapse-free-survival, NRM non-relapse mortality, relapse, severe cGvHD and severe aGvHD

Supplemental table 7. Regression analyses – all patients transplanted after 2005 and with a center-follow up of 50%, n = 7739

	Cox regression regarding overall survival (OS)			**Additive proportional hazards model regarding excess mortality+**		
Covariate	**Total FU*** **HR [95%CI]**	**First year of FU*** **HR [95%CI]**	**Years 1+ of FU*** **HR [95%CI]**	**Total FU*** **HR [95%CI]**	**First year of FU*** **HR [95%CI]**	**Years 1+ of FU*** **HR [95%CI]**
Age group **ref. 60-69**	1	1	1	1	1	1
70-79	**1.21 [1.12-1.31], p<0.001**	**1.22 [1.11-1.34], p<0.001**	**1.2 [1.03-1.38], p=0.016**	**1.18 [1.08-1.28], p<0.001**	**1.21 [1.1-1.34], p<0.001**	**1.06 [0.88-1.28], p=0.56**
Disease, **ref. acute leukemia**	1	1	1	1	1	1
CLL	0.61 [0.51-0.74], p<0.001	0.56 [0.44-0.71], p<0.001	0.73 [0.55-0.97], p=0.032	0.55 [0.44-0.68], p<0.001	0.54 [0.42-0.69], p<0.001	0.58 [0.39-0.87], p=0.009
CML	0.78 [0.59-1.04], p=0.09	0.82 [0.58-1.15], p=0.24	0.71 [0.42-1.19], p=0.19	0.75 [0.55-1.03], p=0.08	0.79 [0.56-1.12], p=0.19	0.64 [0.31-1.3], p=0.21
Lymphoma	1.11 [0.99-1.24], p=0.07	1.21 [1.07-1.38], p=0.003	0.87 [0.7-1.09], p=0.23	1.14 [1.01-1.28], p=0.038	1.23 [1.07-1.4], p=0.003	0.84 [0.63-1.11], p=0.23
MDS/MPN	0.76 [0.7-0.82], p<0.001	0.76 [0.69-0.83], p<0.001	0.78 [0.68-0.9], p<0.001	0.74 [0.68-0.81], p<0.001	0.74 [0.67-0.81], p<0.001	0.77 [0.65-0.92], p=0.004
Plasma cell disorders	0.98 [0.85-1.12], p=0.75	0.82 [0.69-0.99], p=0.036	1.3 [1.05-1.63], p=0.018	0.87 [0.74-1.02], p=0.09	0.81 [0.68-0.98], p=0.031	1.04 [0.78-1.4], p=0.77
Others	1.06 [0.9-1.24], p=0.5	0.99 [0.81-1.21], p=0.93	1.23 [0.93-1.62], p=0.15	1.04 [0.87-1.23], p=0.68	0.99 [0.81-1.21], p=0.89	1.23 [0.88-1.72], p=0.22
Sex ref. female	1	1	1	1	1	1
male	1.08 [1.01-1.14], p=0.015	1.04 [0.97-1.12], p=0.31	1.15 [1.04-1.28], p=0.009	1.06 [0.99-1.13], p=0.11	1.03 [0.96-1.11], p=0.45	1.14 [1-1.3], p=0.06
Comorbidity- **ref. No**	1	1	1	1	1	1

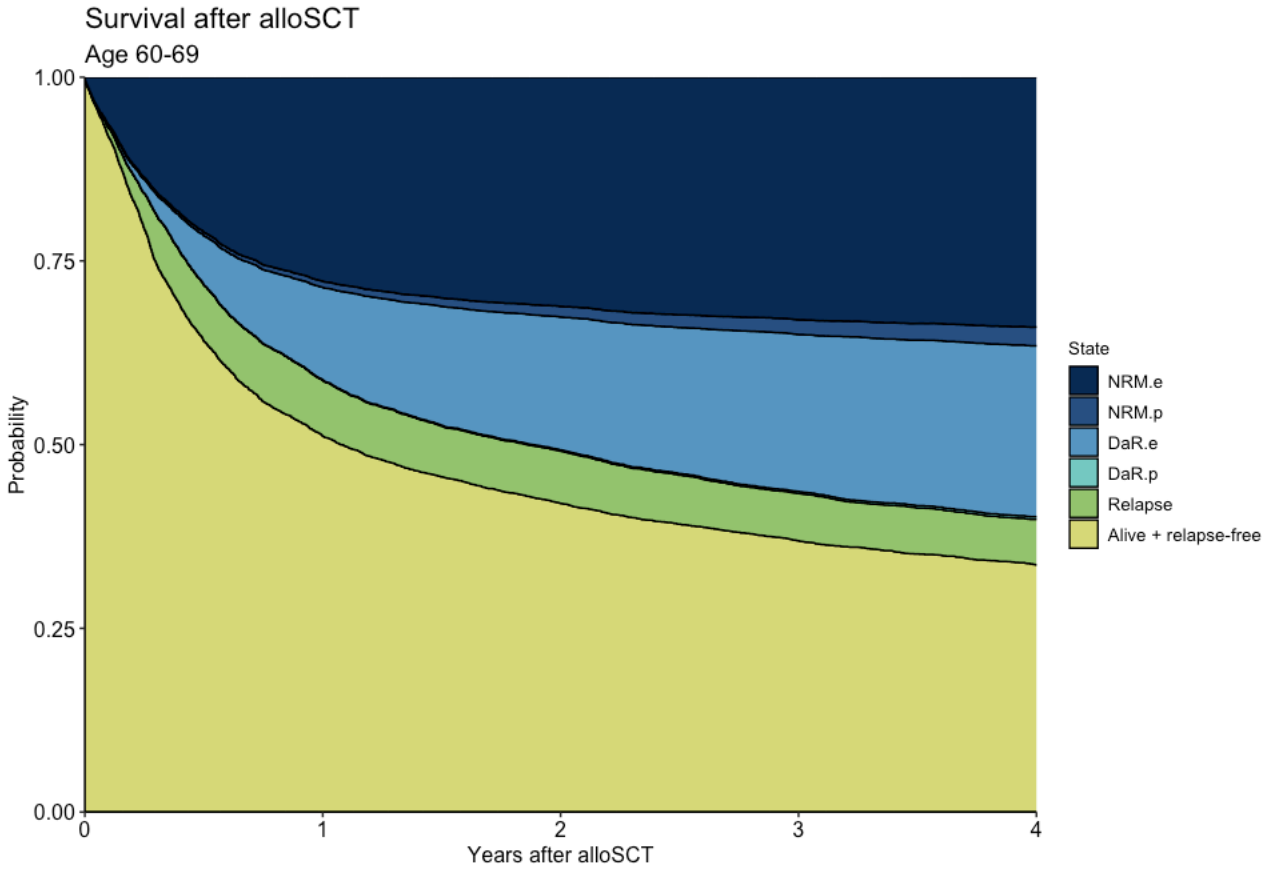
	Cox regression regarding overall survival (OS)			Additive proportional hazards model regarding excess mortality+		
Covariate	**Total FU*** **HR [95%CI]**	**First year of FU*** **HR [95%CI]**	**Years 1+ of FU*** **HR [95%CI]**	**Total FU*** **HR [95%CI]**	**First year of FU*** **HR [95%CI]**	**Years 1+ of FU*** **HR [95%CI]**
Yes	1.16 [1.07-1.26], p<0.001	1.2 [1.09-1.32], p<0.001	1.08 [0.95-1.23], p=0.25	1.18 [1.07-1.31], p=0.002	1.21 [1.07-1.37], p=0.004	1.08 [0.92-1.26], p=0.33
TCI, **ref. high**	1	1	1	1	1	1
Intermediate	0.97 [0.79-1.19], p=0.76	0.99 [0.76-1.28], p=0.91	0.94 [0.67-1.32], p=0.72	0.95 [0.76-1.19], p=0.65	0.95 [0.71-1.27], p=0.71	0.95 [0.61-1.49], p=0.83
Low	0.93 [0.75-1.16], p=0.54	0.97 [0.74-1.28], p=0.84	0.87 [0.61-1.23], p=0.42	0.93 [0.73-1.19], p=0.58	0.95 [0.68-1.32], p=0.75	0.88 [0.55-1.41], p=0.59
Karnofsky Pef. Index, **ref. 90-100**	1	1	1	1	1	1
80	1.25 [1.17-1.34], p<0.001	1.3 [1.19-1.41], p<0.001	1.17 [1.03-1.32], p=0.013	1.29 [1.19-1.4], p<0.001	1.32 [1.2-1.45], p<0.001	1.19 [1.02-1.39], p=0.03
<80	1.83 [1.66-2.03], p<0.001	1.91 [1.7-2.15], p<0.001	1.61 [1.31-1.98], p<0.001	1.91 [1.71-2.12], p<0.001	1.99 [1.77-2.24], p<0.001	1.58 [1.19-2.1], p=0.002
CMV relation, **ref. both IgG negative**	1	1	1	1	1	1
Both positive	1.15 [1.07-1.24], p<0.001	1.2 [1.1-1.32], p<0.001	1.05 [0.93-1.2], p=0.43	1.18 [1.09-1.28], p<0.001	1.22 [1.11-1.34], p<0.001	1.07 [0.91-1.26], p=0.4
Patient neg. donor pos.	1.12 [0.99-1.26], p=0.07	1.13 [0.97-1.3], p=0.11	1.09 [0.89-1.33], p=0.39	1.12 [0.98-1.27], p=0.09	1.13 [0.97-1.31], p=0.11	1.09 [0.85-1.41], p=0.49
Patient pos. donor neg.	1.25 [1.15-1.36], p<0.001	1.31 [1.18-1.46], p<0.001	1.11 [0.95-1.29], p=0.18	1.31 [1.19-1.45], p<0.001	1.35 [1.21-1.5], p<0.001	1.2 [0.99-1.46], p=0.07
Donor Type, **ref. related**	1	1	1	1	1	1

	Cox regression regarding overall survival (OS)			Additive proportional hazards model regarding excess mortality+		
Covariate	**Total FU*** **HR [95%CI]**	**First year of FU*** **HR [95%CI]**	**Years 1+ of FU*** **HR [95%CI]**	**Total FU*** **HR [95%CI]**	**First year of FU*** **HR [95%CI]**	**Years 1+ of FU*** **HR [95%CI]**
Unrelated	1.16 [1.07-1.27], p<0.001	1.2 [1.08-1.33], p<0.001	1.1 [0.95-1.28], p=0.2	1.2 [1.1-1.32], p<0.001	1.21 [1.1-1.35], p<0.001	1.16 [0.98-1.39], p=0.09
Donor Type, HLA-match, **ref. match**	1	1	1	1	1	1
Unmatched	1.34 [1.16-1.54], p<0.001	1.39 [1.19-1.63], p<0.001	1.22 [0.96-1.53], p=0.1	1.42 [1.21-1.67], p<0.001	1.45 [1.21-1.74], p<0.001	1.29 [1.03-1.63], p=0.03
TBI part of conditioning, **ref. No**	1	1	1	1	1	1
Yes	1.14 [1.05-1.25], p=0.003	1.15 [1.03-1.28], p=0.012	1.13 [0.96-1.33], p=0.16	1.13 [1.03-1.25], p=0.012	1.14 [1.03-1.28], p=0.016	1.09 [0.89-1.34], p=0.4
Donor Age, **ref. higher than median**	1	1	1	1	1	1
Lower	0.83 [0.75-0.91], p<0.001	0.83 [0.74-0.94], p=0.002	0.82 [0.69-0.96], p=0.014	0.8 [0.74-0.87], p<0.001	0.82 [0.75-0.9], p<0.001	0.76 [0.65-0.88], p<0.001
Period, **ref. 2006-2012**	1	1	1	1	1	1
2013-2018	0.92 [0.87-0.98], p=0.009	0.87 [0.81-0.94], p<0.001	1.03 [0.93-1.16], p=0.56	0.9 [0.85-0.97], p=0.003	0.87 [0.81-0.94], p<0.001	1.03 [0.9-1.17], p=0.69
Stem cell source, **ref. Bone marrow**	1	1	1	1	1	1
Peripheral Blood	0.9 [0.79-1.03], p=0.13	0.94 [0.81-1.1], p=0.45	0.81 [0.65-1.02], p=0.07	0.94 [0.82-1.07], p=0.34	0.96 [0.82-1.13], p=0.63	0.84 [0.64-1.11], p=0.22
Remission state at HSCT, **ref. no CR**	1	1	1	1	1	1

	Cox regression regarding overall survival (OS)			Additive proportional hazards model regarding excess mortality[+]		
Covariate	**Total FU*** **HR [95%CI]**	**First year of FU*** **HR [95%CI]**	**Years 1+ of FU*** **HR [95%CI]**	**Total FU*** **HR [95%CI]**	**First year of FU*** **HR [95%CI]**	**Years 1+ of FU*** **HR [95%CI]**
Complete remission	0.73 [0.68-0.79], p<0.001	0.68 [0.63-0.75], p<0.001	0.85 [0.75-0.96], p=0.012	0.69 [0.64-0.74], p<0.001	0.67 [0.61-0.73], p<0.001	0.77 [0.66-0.91], p=0.002
Follow-up year 0-1, Hazard	NA	NA	NA	0.49 [0.36-0.65], p<0.001	0.46 [0.31-0.67], p<0.001	Not evaluated
Follow-up year 1-2, Hazard	NA	NA	NA	0.16 [0.11-0.21], p<0.001	NA	0.19 [0.11-0.34], p<0.001
Follow-up year 2-3, Hazard	NA	NA	NA	0.1 [0.07-0.14], p<0.001	NA	0.12 [0.07-0.22], p<0.001
Follow-up year 3-4, Hazard	NA	NA	NA	0.07 [0.05-0.09], p<0.001	NA	0.08 [0.05-0.15], p<0.001
Likelihood Ratio Test	p<0.001	p < 0.001	p < 0.001	NA	NA	NA
[+] See Appendix for model reference						

Values obtained from a multivariable Cox regression model are depicted overall and separately for the first year and subsequent years of follow-up. Likewise, a Cox model was fitted for excess hazard only. An overall p-value of a likelihood ratio test was added. FU follow up.
N = 7739 patients transplanted after 2005 and with a center follow-up of 50%.

Supplemental figure 8.1 – Multistates for all patients 60-69 transplanted after 2005, with a center follow-up of 50%, n = 7739



Supplemental figure 8.2 – Multistates for all patients 70-79 transplanted after 2005, with a center follow-up of 50%, n = 7739