

Stem Cell Transplant for MDS

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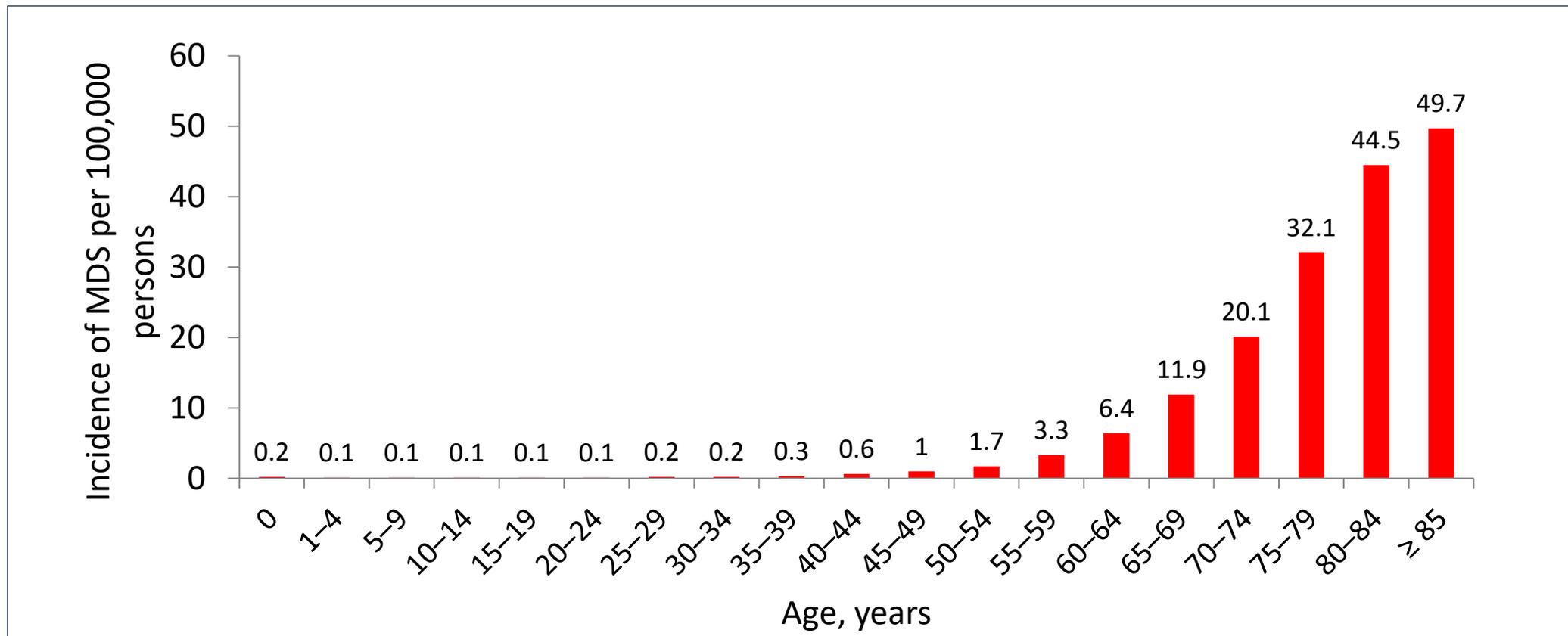


Myelodysplastic Syndrome

- **Malignant disorders characterized by:**
 - Ineffective hematopoiesis (≥ 1 lineage)
 - Variable % of leukemic blasts
- **Median age is 70**
- **30% progress to AML**
- **US incidence: ~15,000 cases annually: Canada: 1500**
- **US prevalence: 35,000 to 55,000: Canada: 4500**
- **Majority present with moderate to severe anemia**

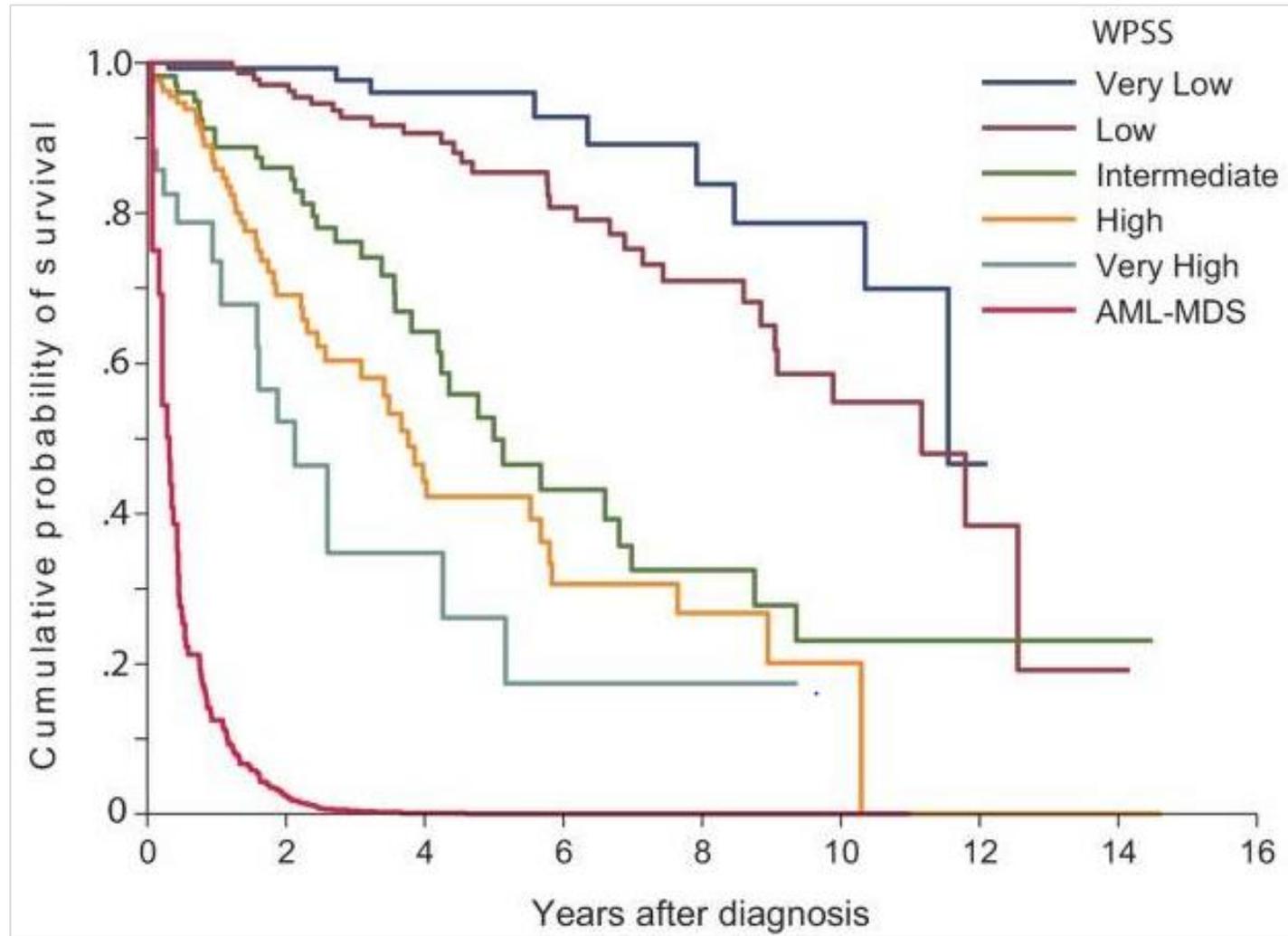
Epidemiology of MDS

- Generally a disease of elderly¹
- Median age at diagnosis is 76 years¹



1. Ma. AM J Med. 2012;125:S2-S5

Overall Survival of MDS Patients



Am J Hematol. 2013 Jul; 88(7): 581-588.

Cytogenetic Scoring System

Table 3. Design of Cytogenetic Scoring System (n = 2,754)*

Prognostic Subgroup	Abnormality					Overall Survival				AML Transformation			
	No. of Patients	%	Single	Double	Complex	Median (months)†	95% CI	HR	95% CI	Median (months)†	95% CI	HR	95% CI
Very good	81	2.9	del(11q) -Y	—	—	60.8	50.3 to NR	0.5†	0.3 to 0.7	NR	121.2 to NR	0.5	0.2 to 1.2
Good (reference)	1,809	65.7	Normal del(5q) del(12p) del(20q)	Including del(5q)	—	48.6	44.6 to 54.3	1.0	0.9 to 1.1	NR	189.0 to NR	1.0	0.9 to 1.2
Intermediate	529	19.2	del(7q) +8 i(17q) +19 Any other Independent clones	Any other	—	26.0	22.1 to 31.0	1.6†	1.4 to 1.8	78.0	42.6 to NR	2.2†	1.8 to 2.7
Poor	148	5.4	inv(3)/t(3q)/ del(3q) -7	Including -7/del(7q)	3	15.8	12.0 to 18.0	2.6†	2.1 to 3.2	21.0	13.4 to 42.2	3.4†	2.5 to 4.6
Very poor	187	6.8	—	—	> 3	5.9	4.9 to 6.9	4.2†	3.4 to 5.2	8.2	6.4 to 15.4	4.9†	3.6 to 6.7

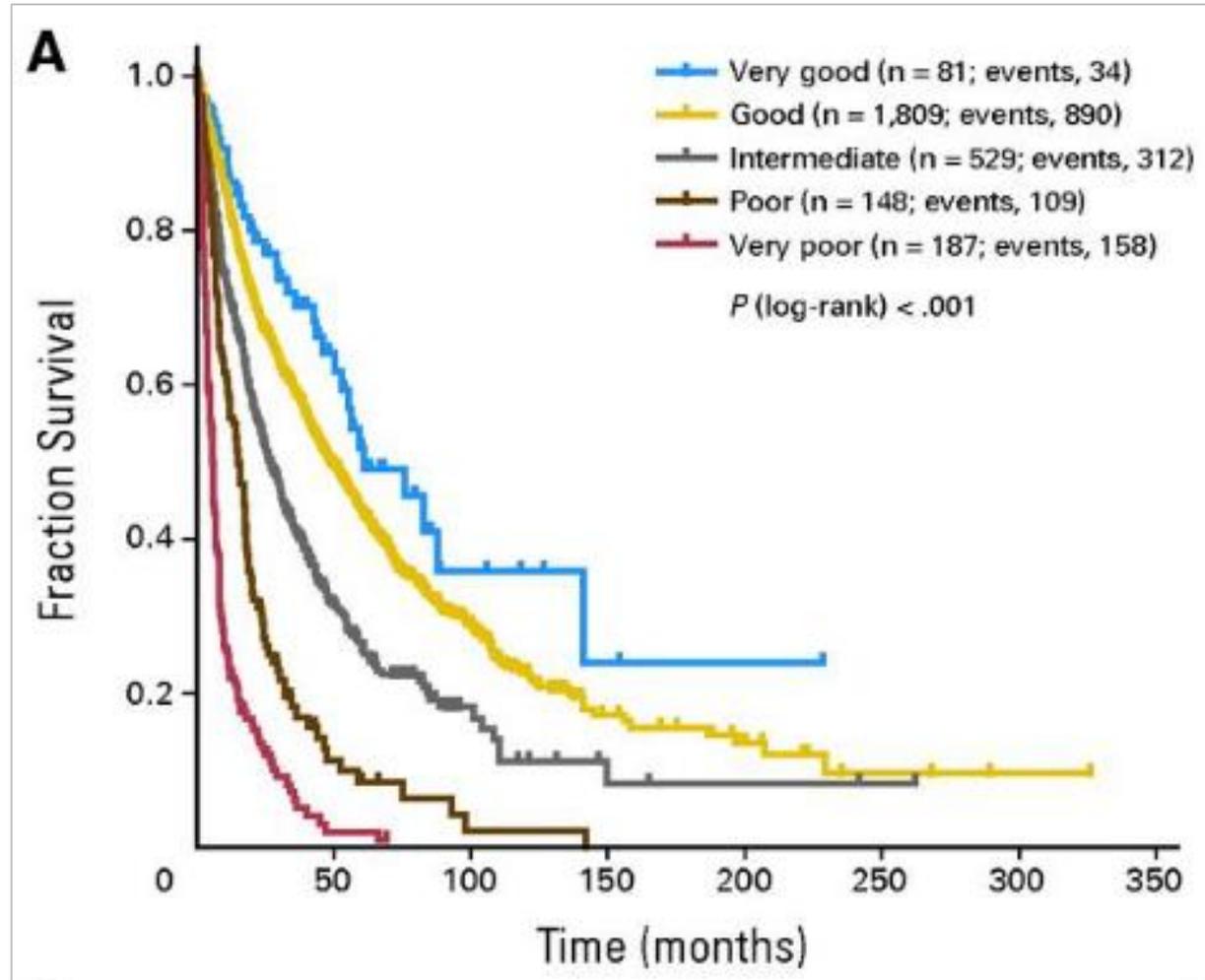
Abbreviations: AML, acute myeloid leukemia; HR, hazard ratio; NR, not reached.

*Patients with complete data.

†P < .01.

J Clin Oncol. 2012 Mar 10;30(8):820-9. doi: 10.1200/JCO.2011.35.6394. Epub 2012 Feb 13.

Fraction Survival



J Clin Oncol. 2012 Mar 10;30(8):820-9. doi: 10.1200/JCO.2011.35.6394. Epub 2012 Feb 13.

IPSS-R Prognostic Score Values

Prognostic variable	0	0.5	1	1.5	2	3	4
Cytogenetics	Very good	–	Good	–	Intermediate	Poor	Very poor
BM blast, %	≤ 2	–	> 2%- < 5%	–	5%-10%	> 10%	–
Hemoglobin	≥ 10	–	8- < 10	< 8	–	–	–
Platelets	≥ 100	50-< 100	< 50	–	–	–	–
ANC	≥ 0.8	< 0.8	–	–	–	–	–



Blood. 2012 Sep 20;120(12):2454-65. Epub 2012 Jun 27.



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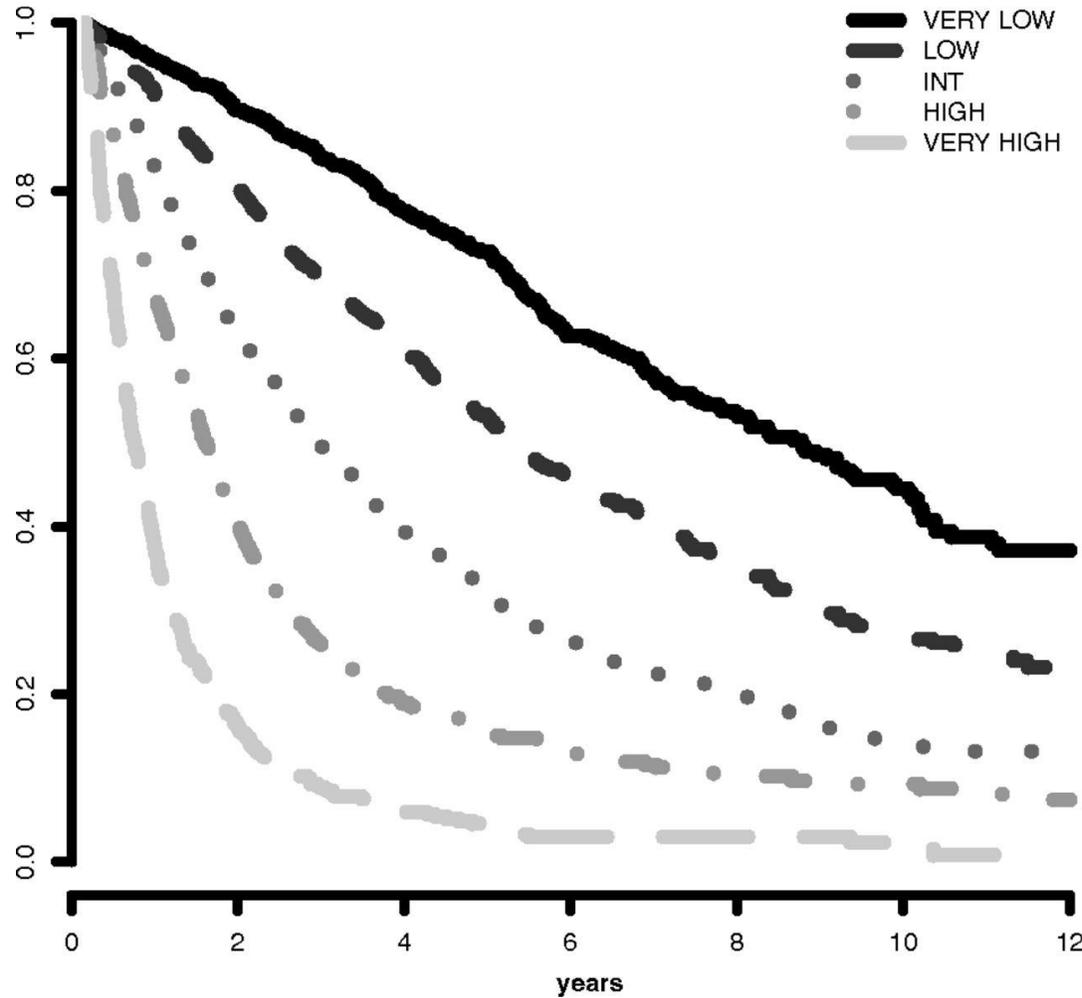


MDS Risk Assessment Calculator

Variables (units) [usual range]	Value
Hemoglobin (g/dL) [4-20] A possible conversion for Hb values: 10 g/dL= 6.2 mmol/L, 8 g/dL= 5.0 mmol/L	<input type="text"/>
Absolute Neutrophil Count (x10⁹/L) [0-15]	<input type="text"/>
Platelets (x10⁹/L) [0-2000]	<input type="text"/>
Bone Marrow Blasts (percent) [0-30]	<input type="text"/>
Cytogenetic Category <input type="radio"/> Very Good <input type="radio"/> Good <input type="radio"/> Intermediate <input type="radio"/> Poor <input type="radio"/> Very Poor	
IPSS-R SCORE	IPSS-R CATEGORY
-	-
<input type="button" value=" > Calculate"/>	
Age-adjusted calculation of risk (IPSS-RA): (only for survival estimation)	
Age <input type="text"/> Years	
IPSS-R SCORE (including age)	IPSS-R CATEGORY (including age)
-	-
<input type="button" value=" > Calculate"/> <input type="button" value=" > Reset Calculator"/>	

<https://www.mds-foundation.org/ipss-r-calculator/>

Survival Based on IPSS-R Prognostic Risk-Based Categories



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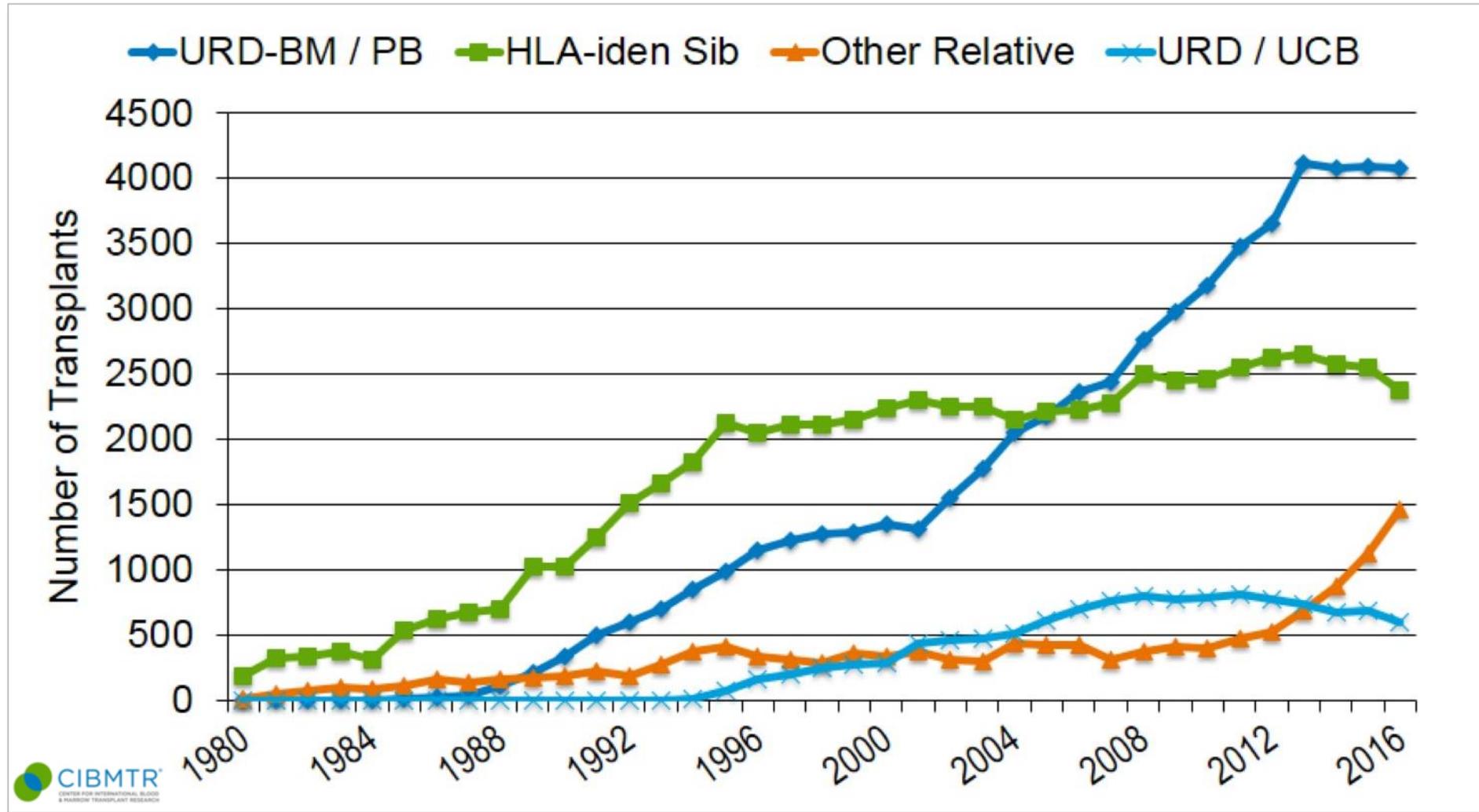


Common Gene Mutations in MDS

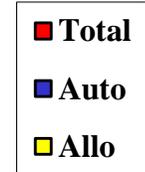
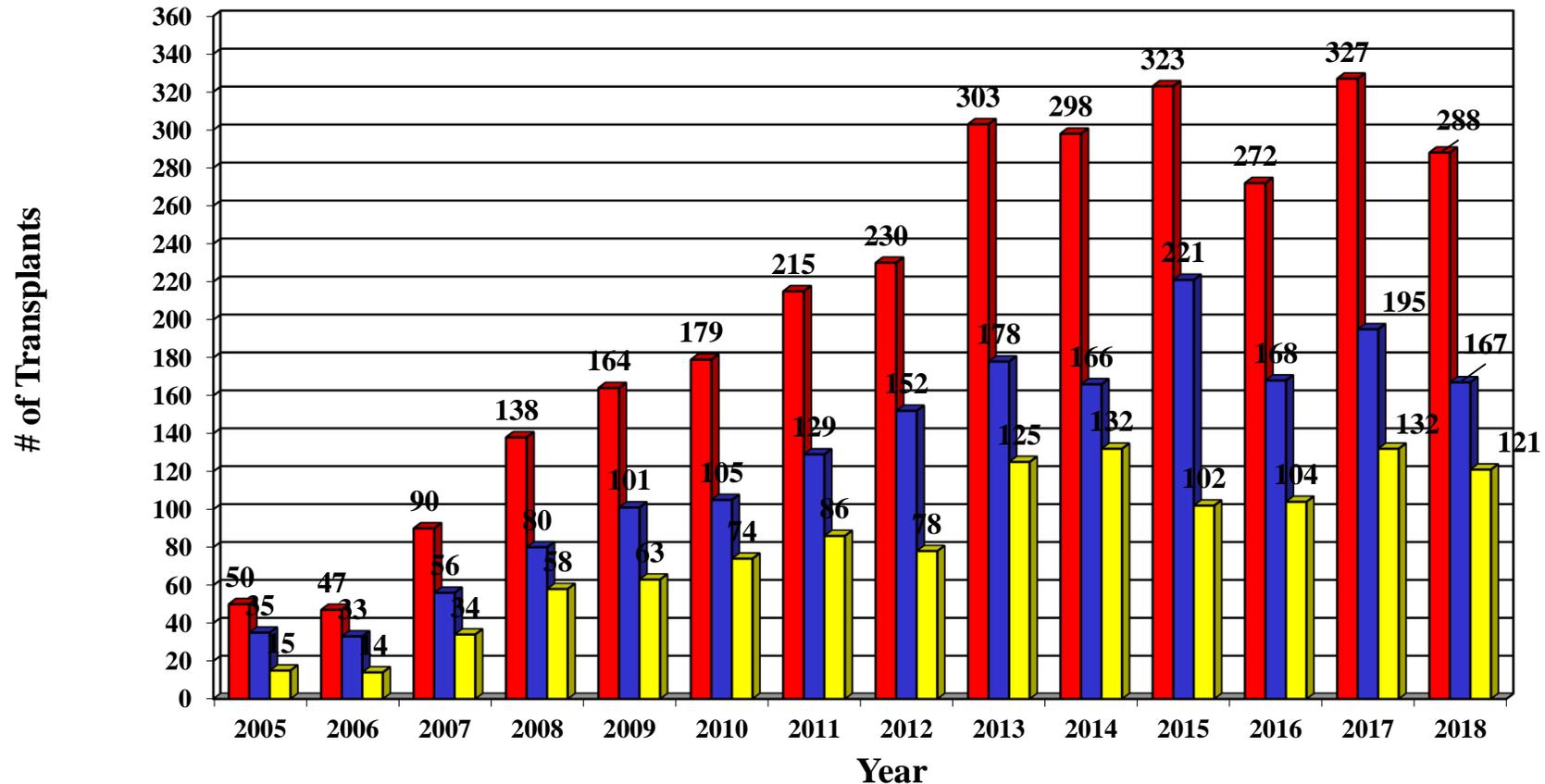
Category	Gene	Frequency	References
RNA splicing	<i>SF3B1</i>	20-35%	Papaemmanuil <i>et al</i> (2011); Yoshida <i>et al</i> (2011)
	<i>SRSF2</i>	10-15%	Thol <i>et al</i> (2012); Arbab Jafari <i>et al</i> (2018)
	<i>U2AF1</i>	5-10%	Thol <i>et al</i> (2012); Graubert <i>et al</i> (2011)
	<i>ZRSR2</i>	<5%	Thol <i>et al</i> (2012); Gill <i>et al</i> (2016)
DNA methylation	<i>TET2</i>	11-26%	Delhommeau <i>et al</i> (2009); Guo <i>et al</i> (2017)
	<i>DNMT3A</i>	7-10%	Lin <i>et al.</i> (2018) Hou <i>et al</i> (2018)
Histone modification	<i>ASXL1</i>	~20%	Haferlach <i>et al</i> (2014); Thol <i>et al</i> (2012)
	<i>EZH2</i>	~5%	Hou <i>et al</i> (2018); Haferlach <i>et al</i> (2014)
DNA transcription	<i>RUNX1</i>	~10%	Cazzola <i>et al</i> (2013); Chen <i>et al</i> (2007)
	<i>TP53*</i>	~5%	Cazzola <i>et al</i> (2013); Sperling <i>et al</i> (2017)
Signal transduction	<i>NRAS</i>	<5%	Xu <i>et al</i> (2017); Bejar <i>et al</i> (2011)
	<i>KRAS</i>	<5%	Cazzola <i>et al</i> (2013); Bejar <i>et al</i> (2011)
	<i>PTPN11</i>	<5%	Bejar <i>et al</i> (2011); Montalban-Bravo <i>et al</i> (2017a)
Chromatid cohesion	<i>STAG2</i>	<10%	Montalban-Bravo <i>et al</i> (2017a); Gill <i>et al</i> (2016); Cazzola <i>et al</i> (2013)
	<i>RAD21</i>	<5%	Thota <i>et al</i> (2014); Haferlach <i>et al</i> (2014)
	<i>SMC1A</i>	<5%	Thota <i>et al</i> (2014); Matto <i>et al</i> (2015)
	<i>SMC3</i>	<5%	Gill <i>et al</i> (2016); Thota <i>et al</i> (2014)

Br J Haematol. 2019 Oct 1. doi: 10.1111/bjh.16212

Allogeneic HCT Recipients in the US, by Donor Type

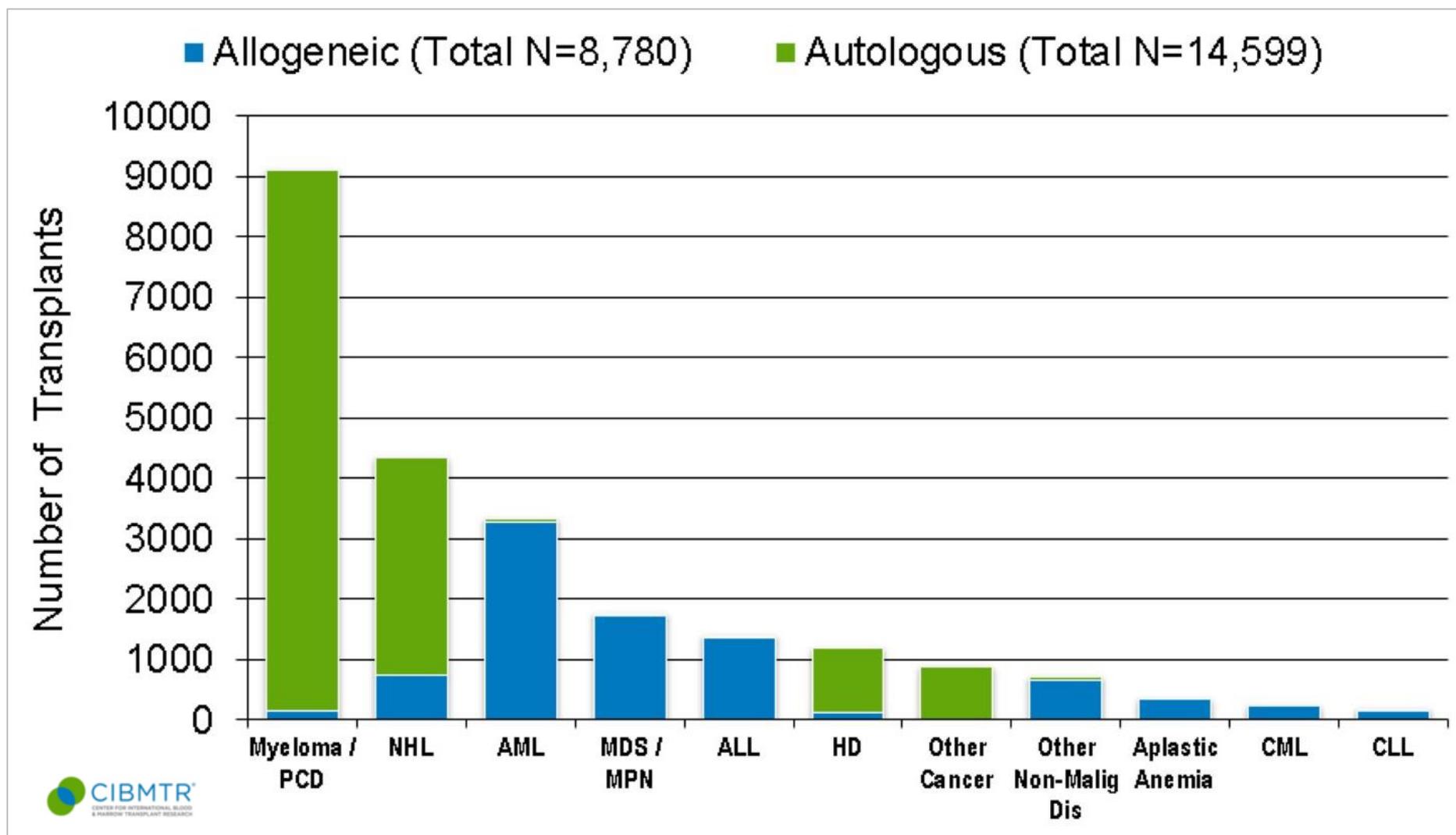


Blood & Marrow Transplant – Annual Volume (CY)



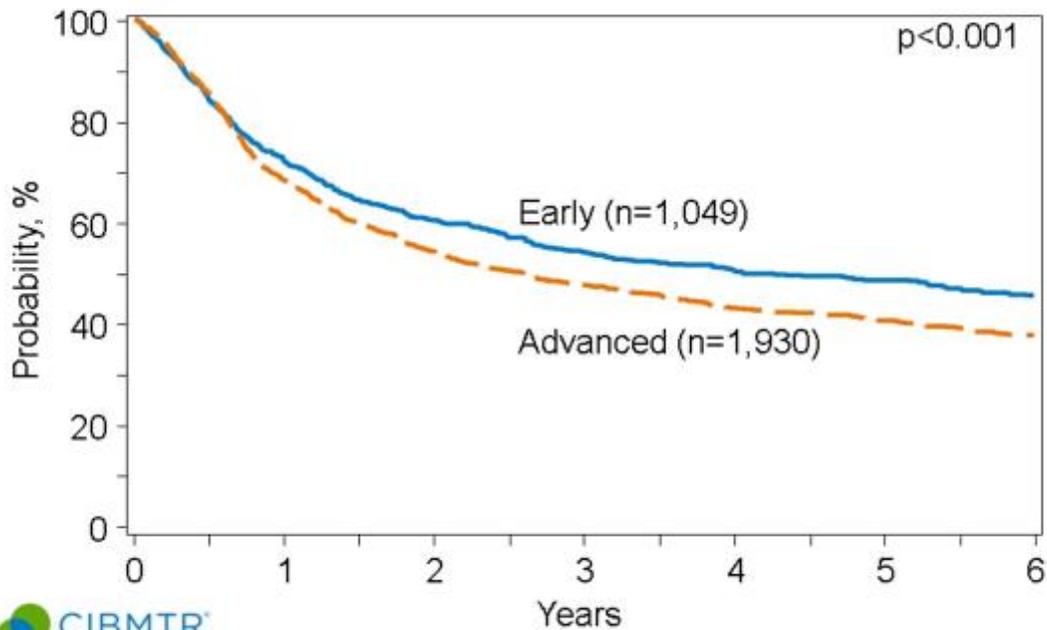
CY18 Volume	
Avg. Monthly	24.0
Range	18-35

Indication for HCT in the US, 2017

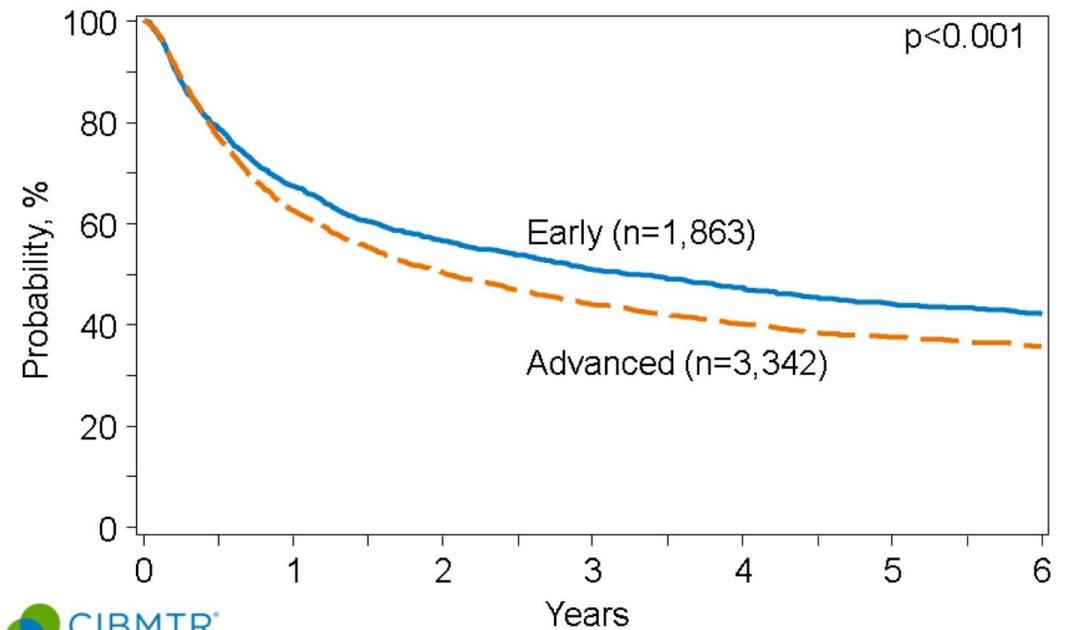


Transplant Survival Outcomes

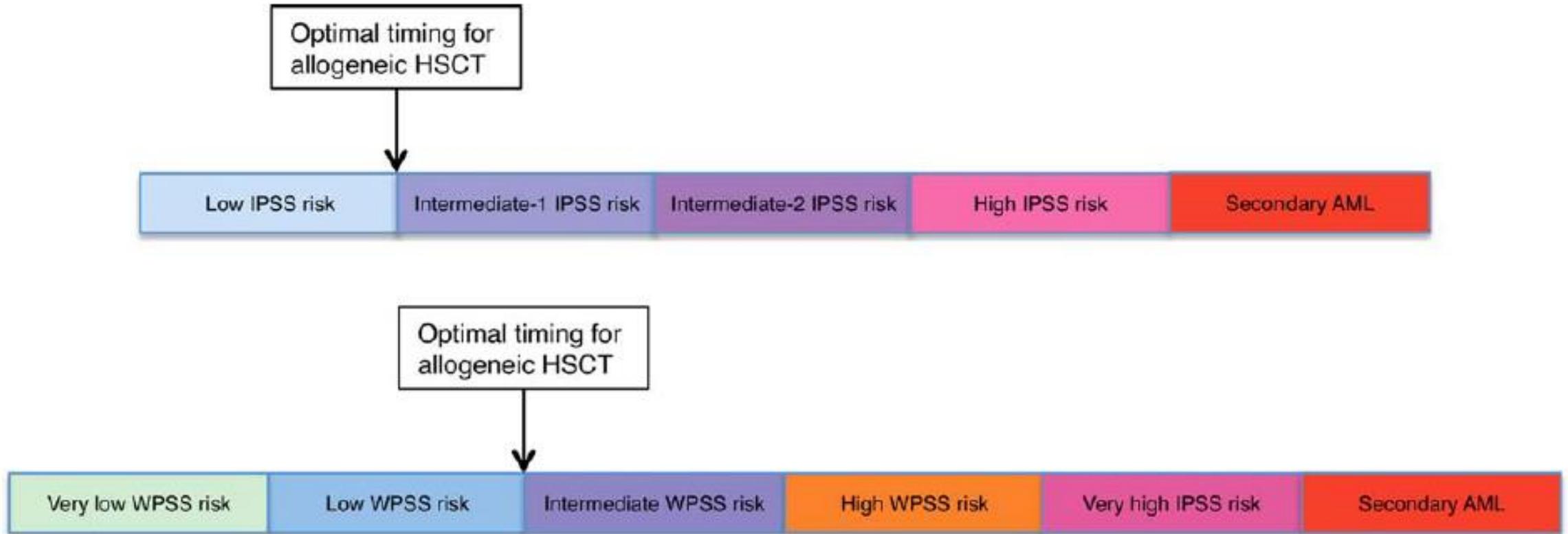
Survival after HLA-Matched Sibling HCT for Myelodysplastic Syndrome (MDS), 2006-2016



Survival after Unrelated Donor HCT for Myelodysplastic Syndrome (MDS), 2006-2016

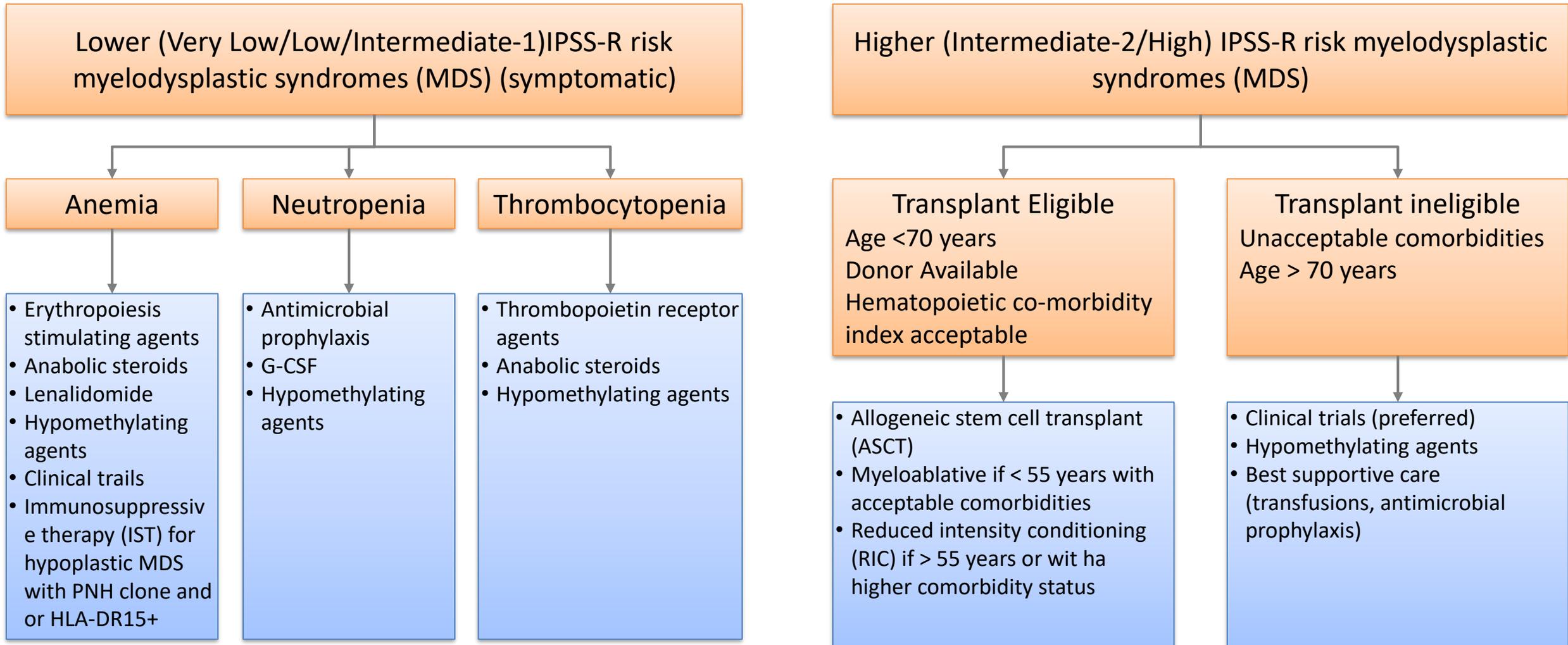


Natural history of MDS according to IPSS or WPSS risk stratification



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Risk-adapted treatment approach for management of MDS



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Thank You!



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