Current Prognostication in Primary Myelofibrosis

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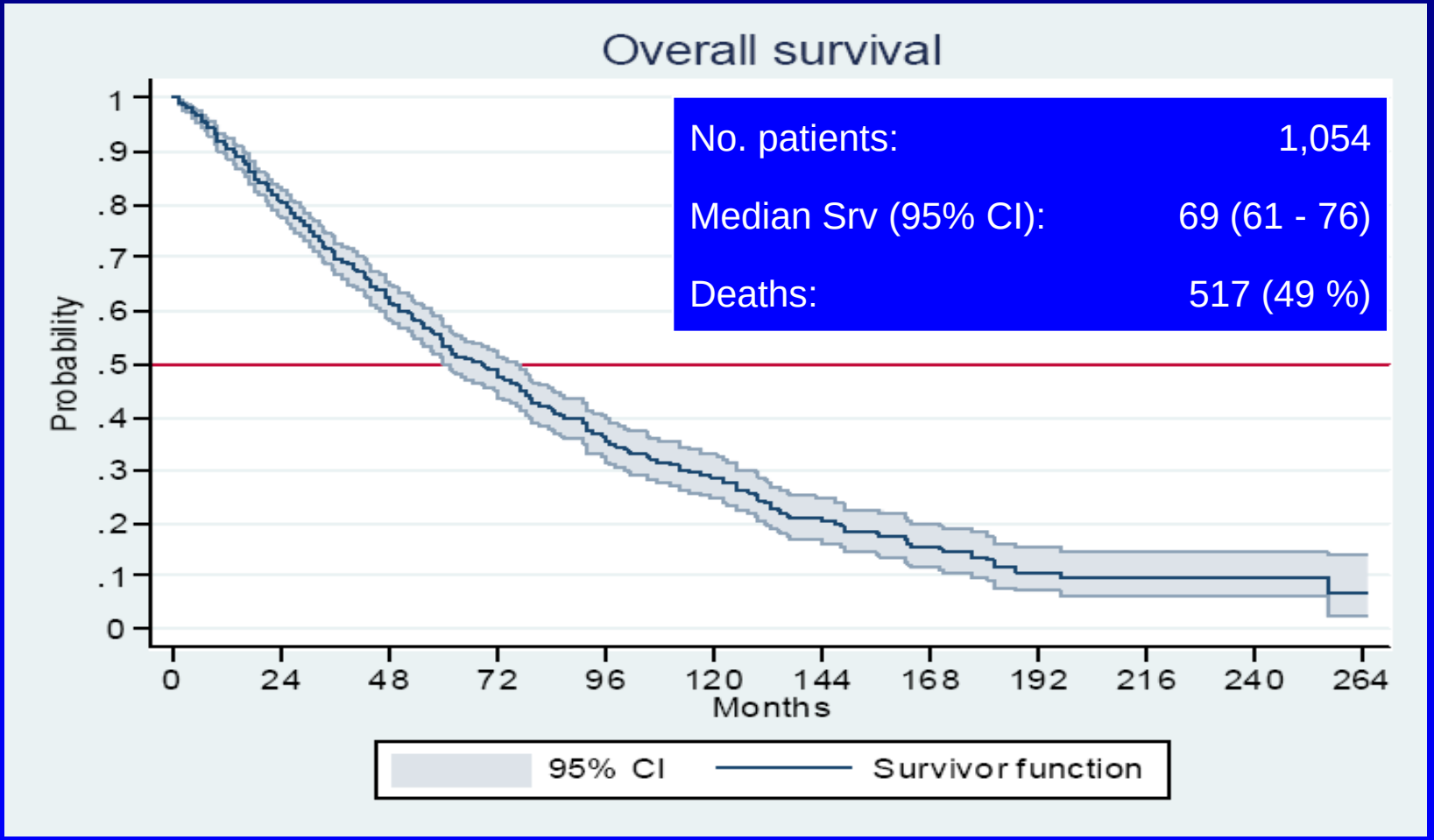
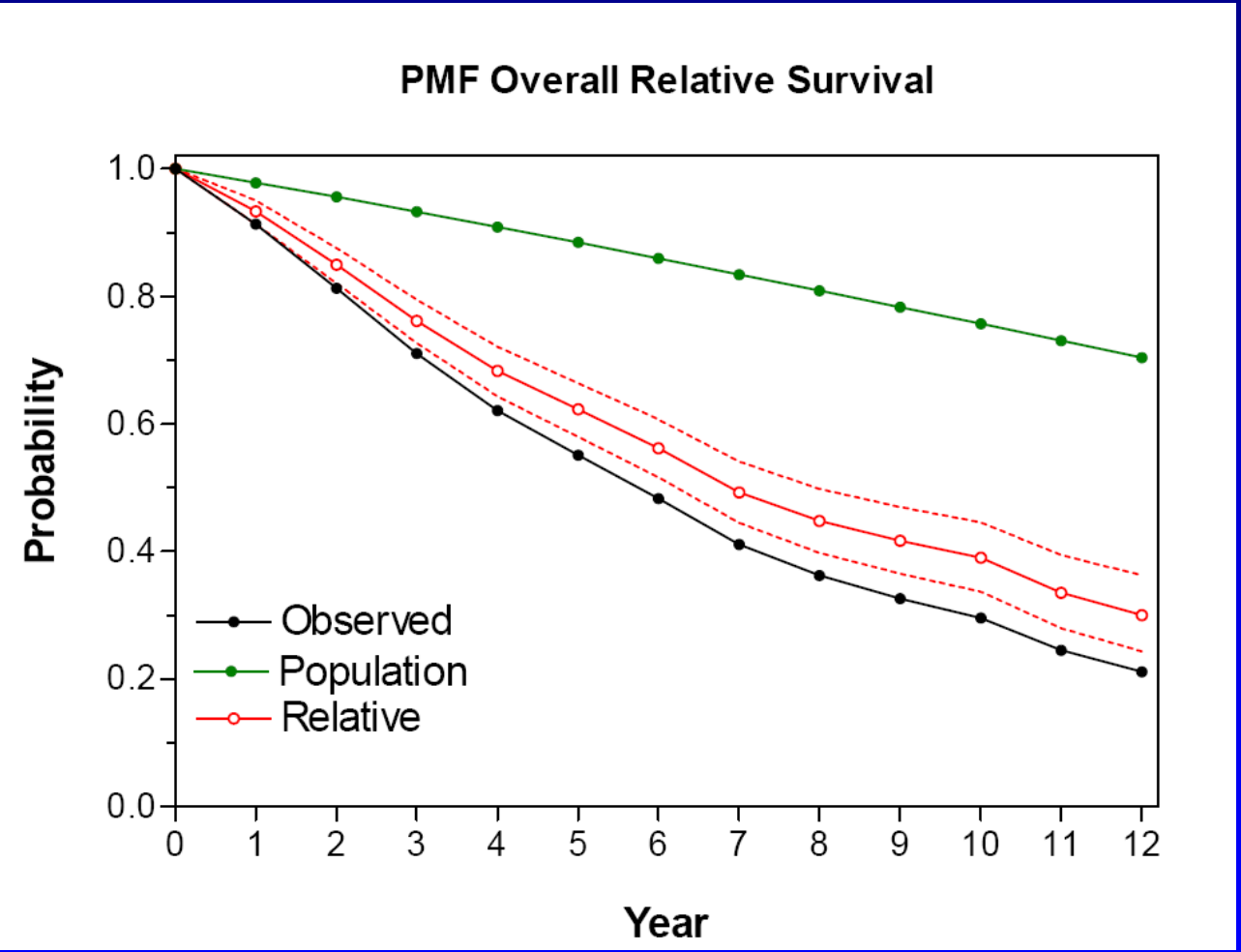
Survival in PMF



Cervantes *et al.*, Blood 2009

Relative Survival in PMF



Cervantes *et al.*, Blood *2009*

Main Prognostic Factors in PMF

- Hb < 10 g/dL
- Constitutional symptoms
- Older age
- Leukocyte counts
- Blood blasts
- Abnormal karyotype

Dupriez´s Prognostic Score

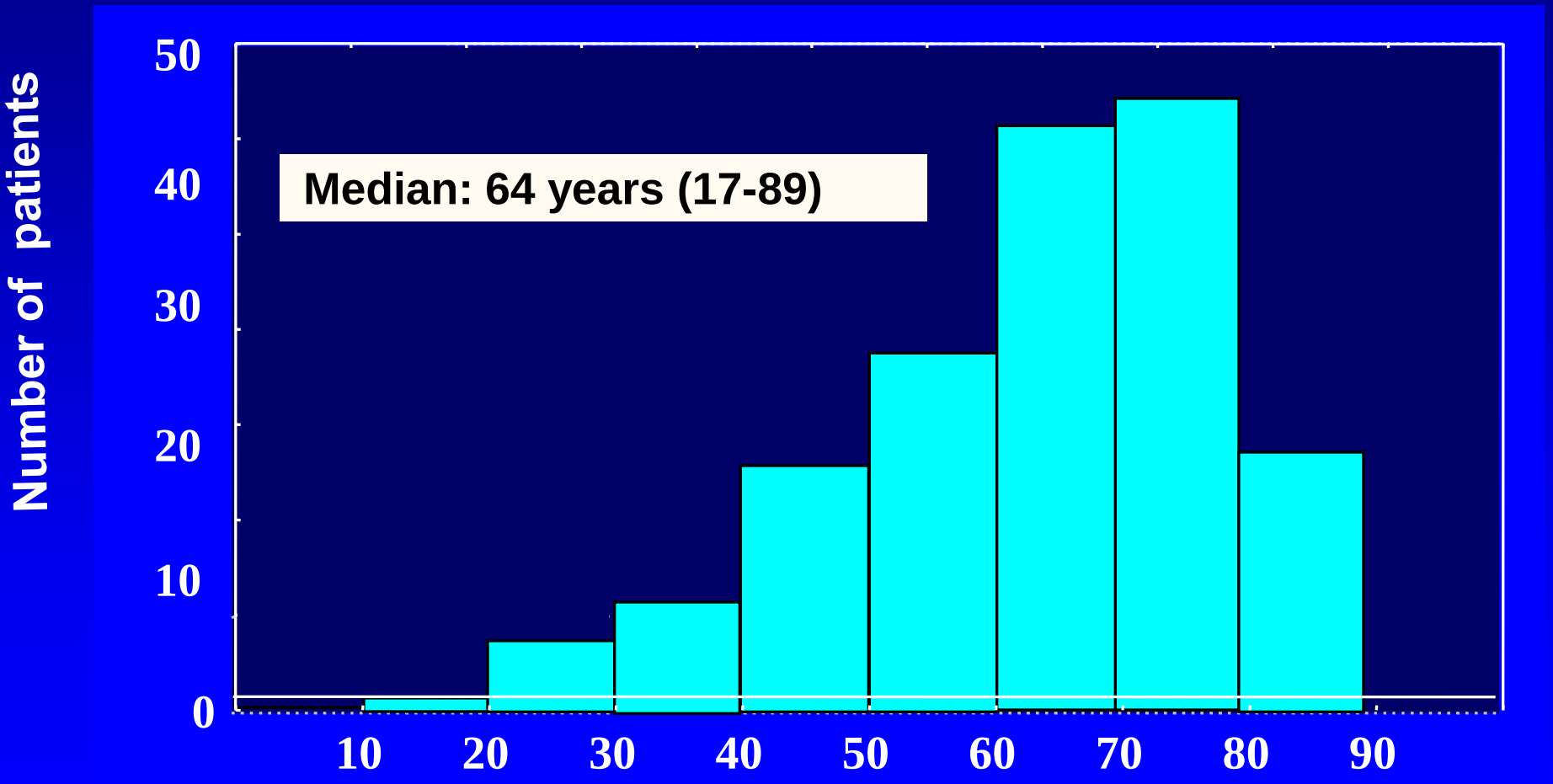
Adverse factors

- Hb < 10 g/dL
- WBC < 4 or > 30 x 10^9/L

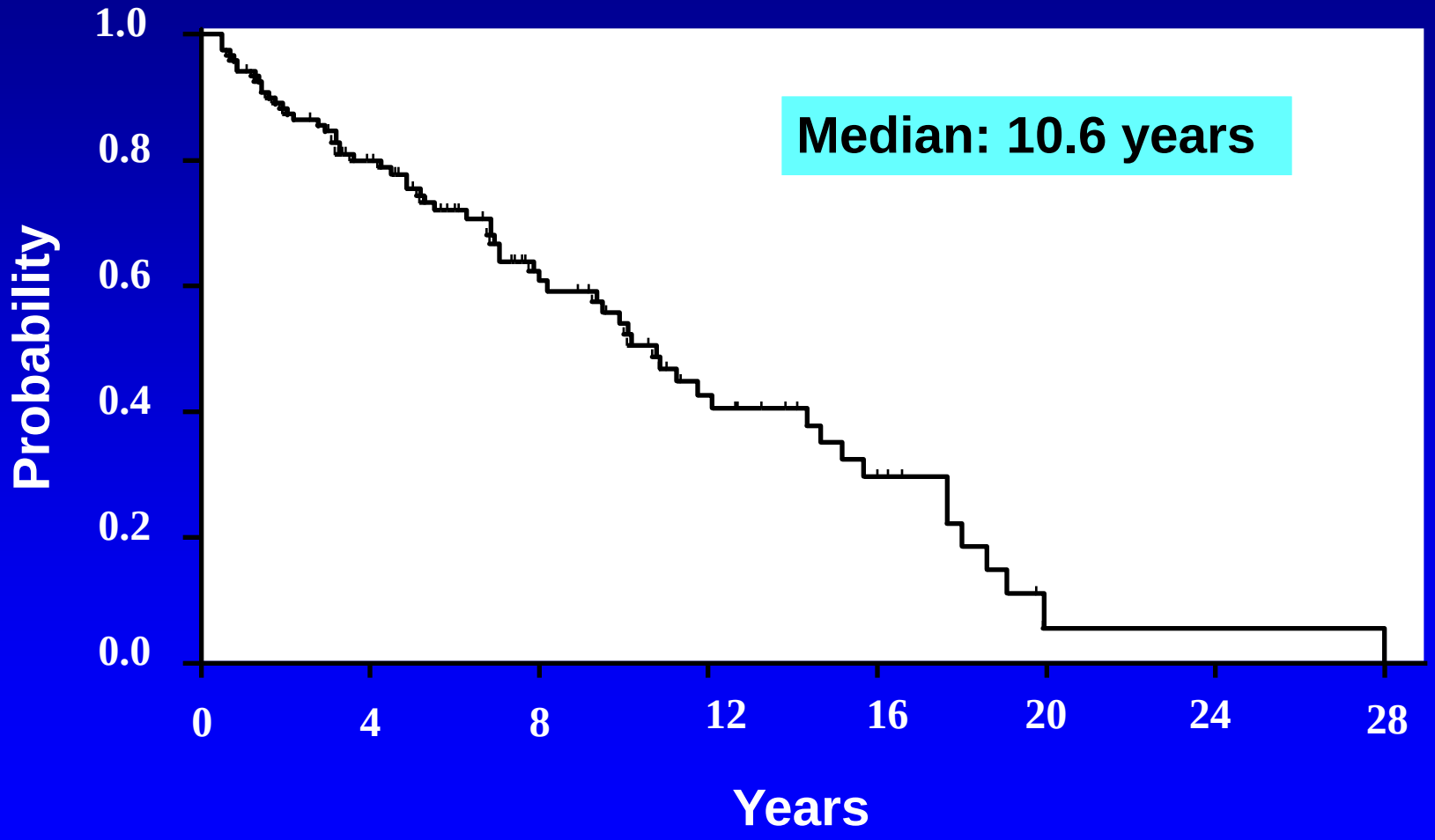
Prognostic groups	Median survival
• Low risk: 0 factors	93 months
• Intermediate risk: 1 factor	26 months
• High risk: 2 factors	13 months

Dupriez *et al*., Blood 1996

Primary Myelofibrosis: Age Distribution (n= 173)

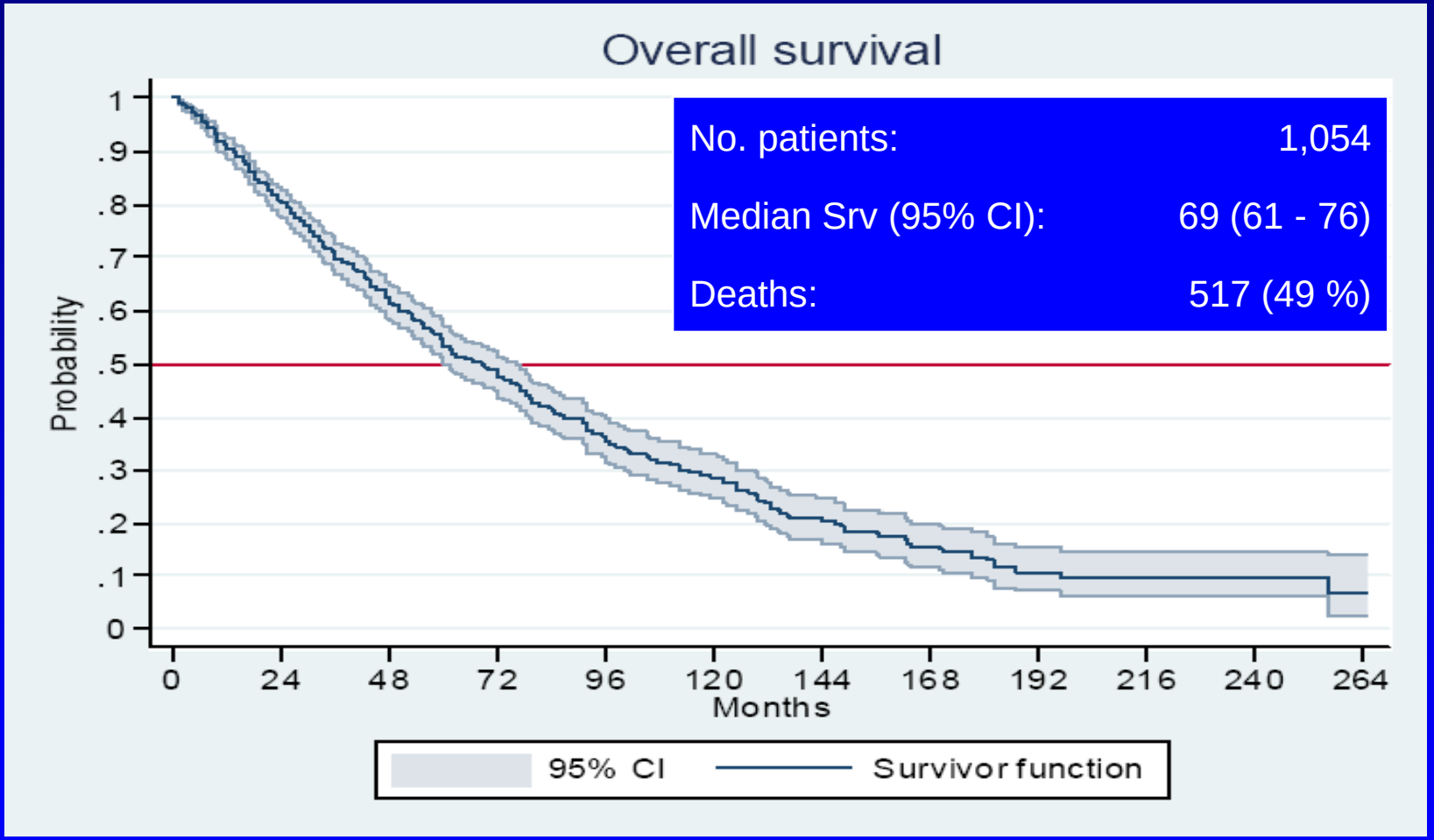


Survival of PMF Patients ≤ 55 years (n= 121)



Cervantes *et al*., Br J Haematol 1998

Survival in PMF



Cervantes *et al.*, Blood 2009

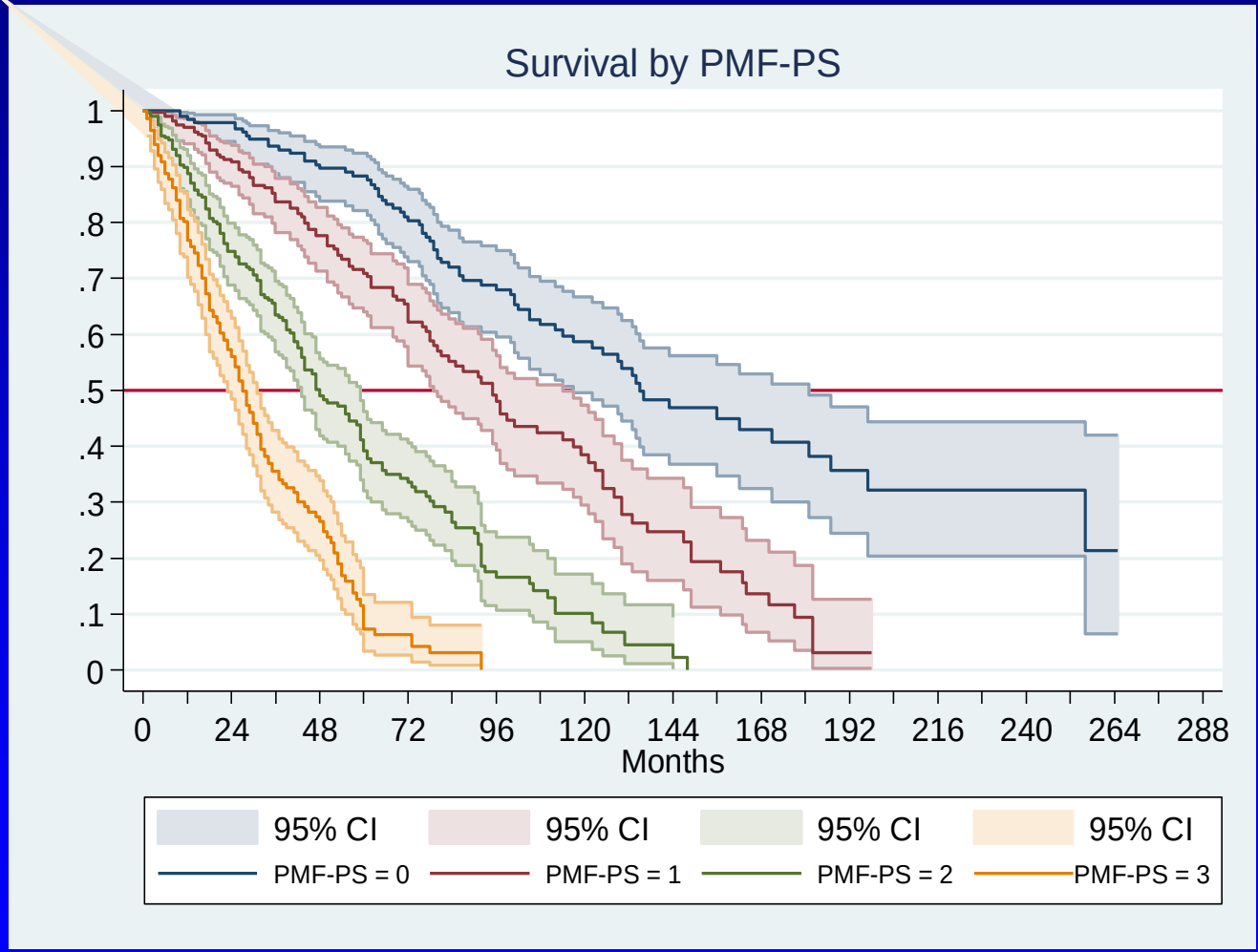
IPSS: Risk classification of PMF at presentation

Prognostic factors

- Age > 65 years
- Constitutional symptoms
- Hb < 10 g/dL
- Leukocytes > 25 x 10^9/L
- Blood blasts ≥ 1%

Risk groups

• Low	0
• Intermediate-1	1
• Intermediate-2	2
• High	≥ 3



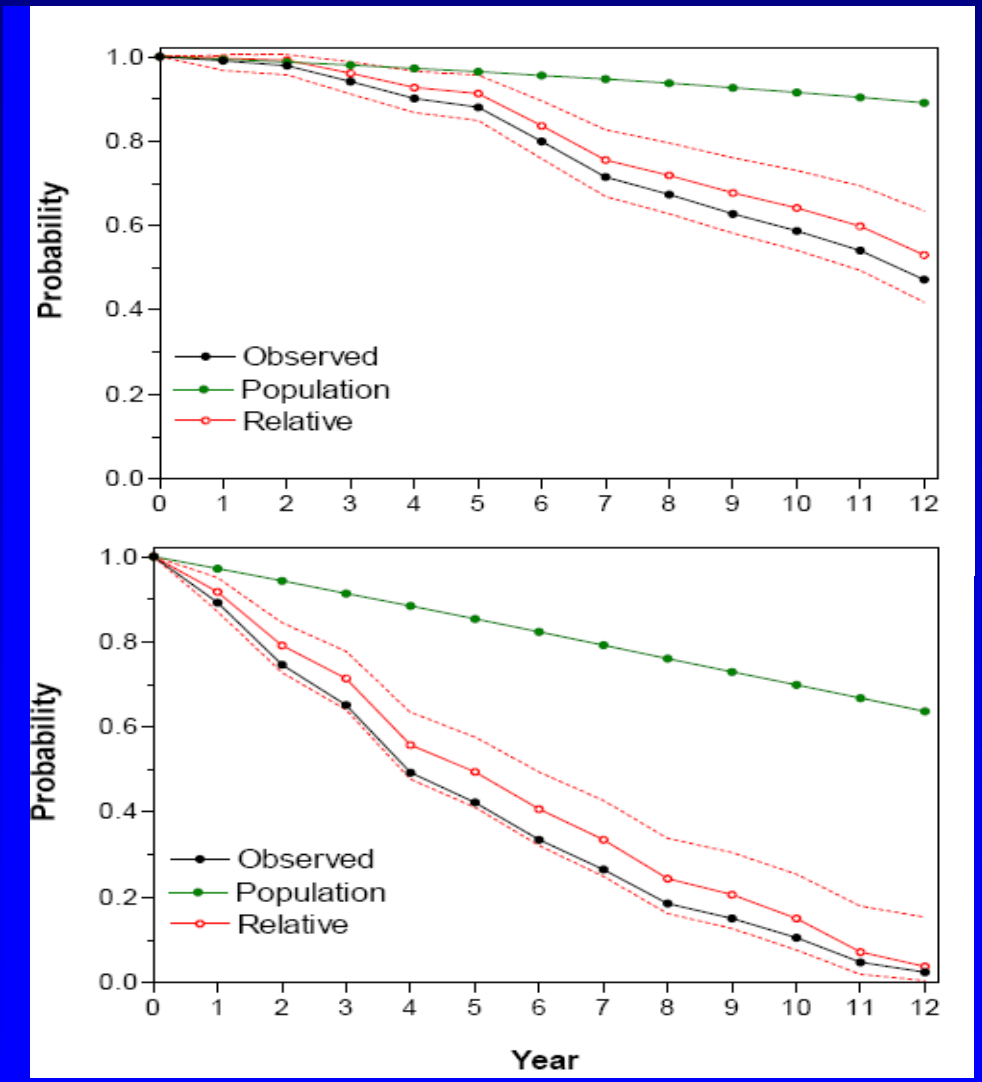
Cervantes *et al.*, Blood 2009;113:2895-2901

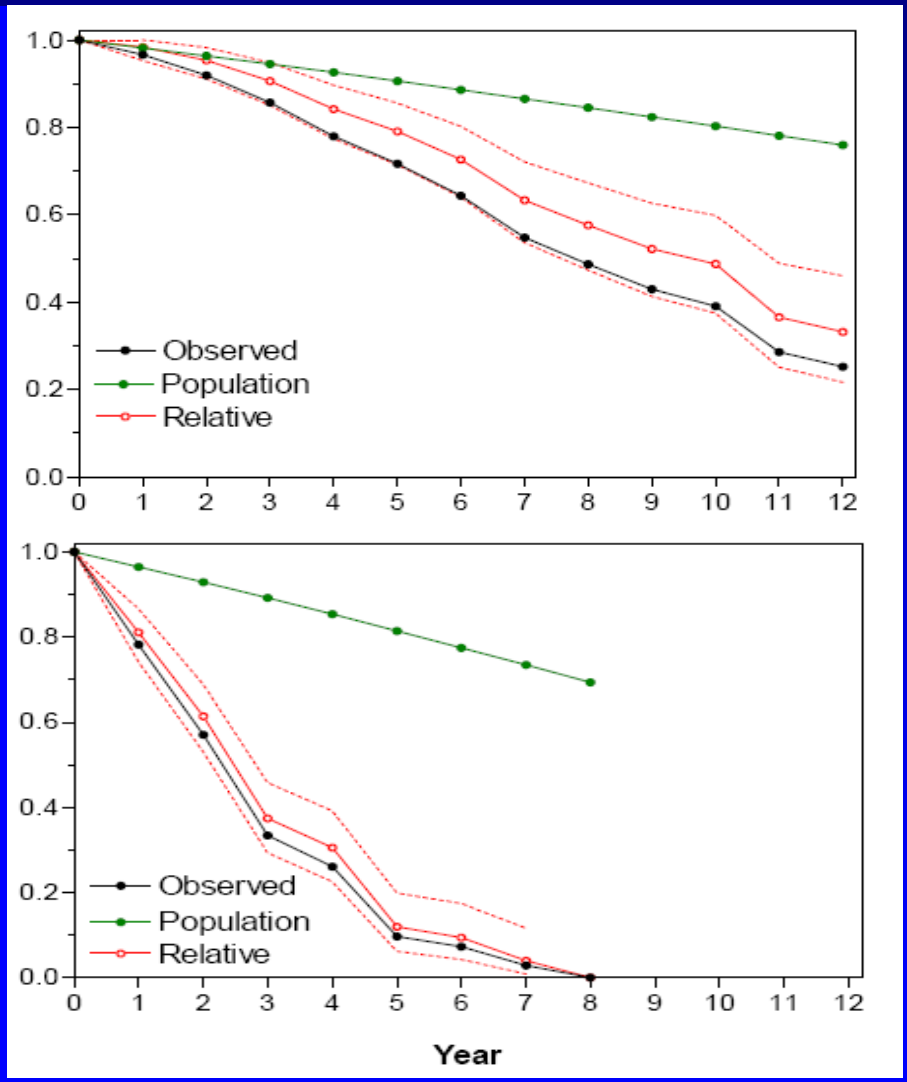
PMF- Prognostic groups

Risk Group	No. factors	No. cases (%)	Median Srv (95% CI)	No. deaths (%)
Low	0	224 (22 %)	135 (117 - 181)	72 (32 %)
Interm. 1	1	229 (29 %)	95 (79 - 114)	114 (50 %)
Interm. 2	2	282 (28 %)	48 (43 - 59)	161 (71 %)
High	≥ 3	202 (21 %)	27 (23 - 31)	147 (73 %)

Cervantes *et al.*, Blood *2009*

PMF: Relative Survival by Risk Group





Cervantes *et al.*, Blood 2009

Dynamic IPSS (DIPSS) in Overall PMF Patients: Weight of Variables and Risk Groups

Table 3. DIPSS for survival in primary myelofibrosis

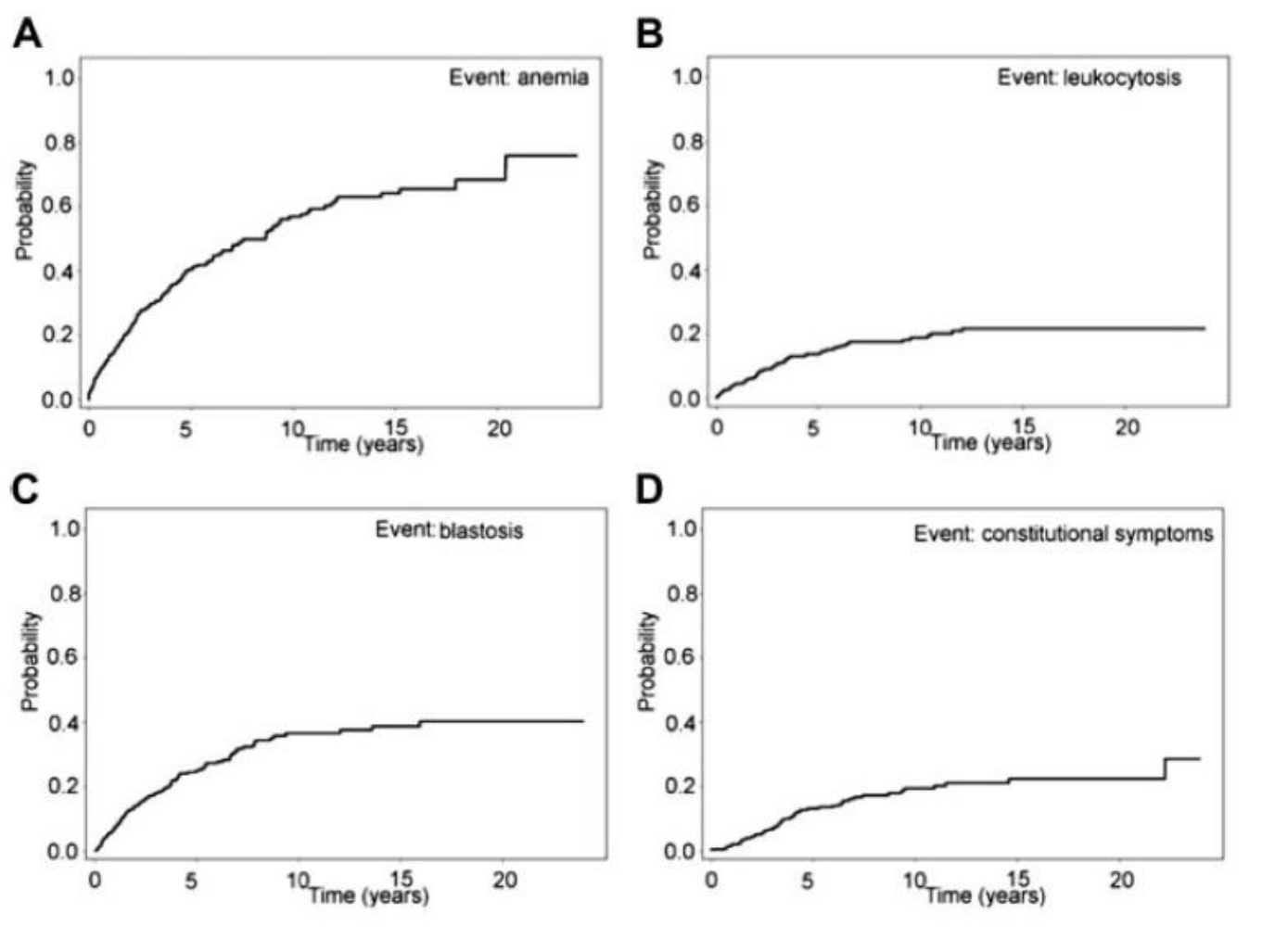
	Value		
Prognostic variable	**0**	**1**	**2**
Age, y	≤ 65	> 65	
White blood cell count, $\times 10^9$/L	≤ 25	> 25	
Hemoglobin, g/dL	≥ 10		< 10
Peripheral blood blast, %	< 1	≥ 1	
Constitutional symptoms, Y/N	N	Y	

The risk category is obtained adding up the values of each prognostic variable. Risk categories are defined as low: 0; intermediate-1: 1 or 2; intermediate-2: 3 or 4; and high: 5 or 6.

DIPSS indicates Dynamic International Prognostic Scoring System.

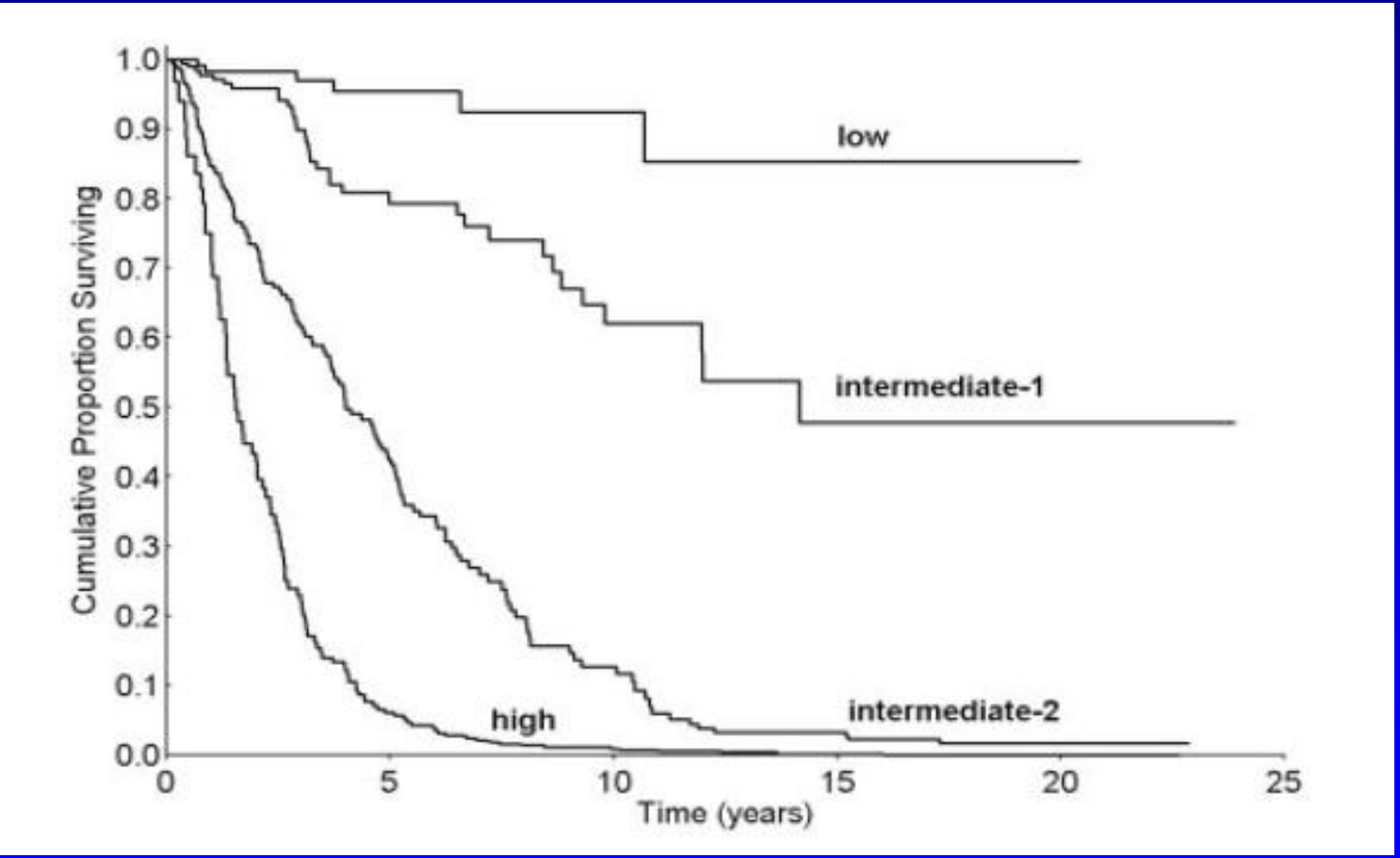
Passamonti *et al.*, Blood 2010

Dynamic International Prognostic Scoring System: Time of Appearance of the Risk Factors



Passamonti *et al.*, Blood 2010

Dynamic International Prognostic Scoring System: Survival by risk group (overall series)



Passamonti *et al.*, Blood 2010

DIPSS in PMF Patients < 65 years: Weight of Variables and Risk Groups

Table 4. Age-adjusted DIPSS for survival in primary myelofibrosis

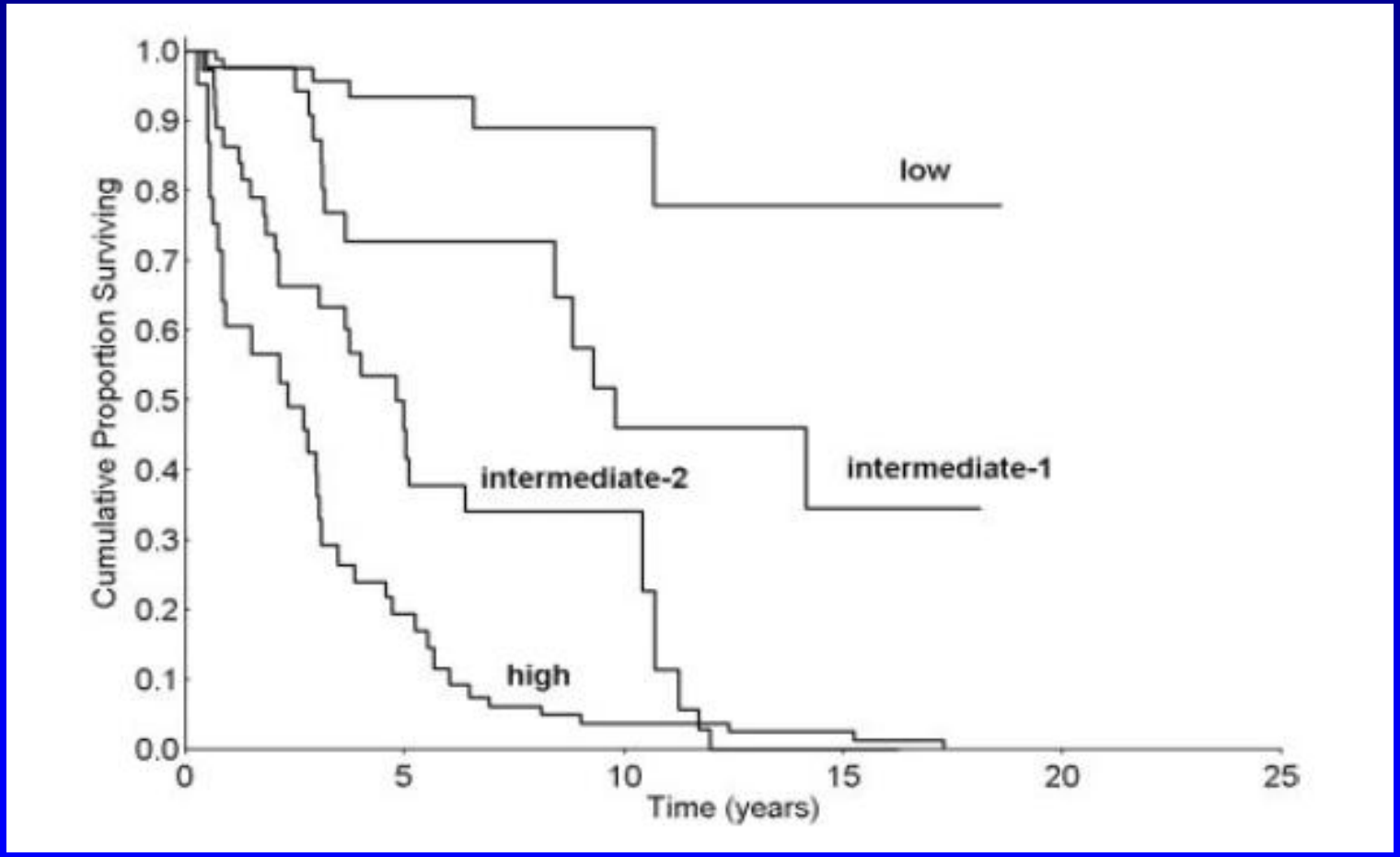
	Value		
Prognostic variable	**0**	**1**	**2**
White blood cell count, $\times 10^9$/L	≤ 25	> 25	
Hemoglobin, g/dL	≥ 10		< 10
Peripheral blood blast, %	< 1		≥ 1
Constitutional symptoms, Y/N	N		Y

The risk category is obtained adding up the values of each prognostic variable. Risk categories are defined as low: 0; intermediate-1: 1 or 2; intermediate-2: 3 or 4; and high: more than 4.

DIPSS indicates Dynamic International Prognostic Scoring System.

Passamonti *et al.*, Blood 2010

Survival by DIPSS PMF risk group (patients < 65 years)



Passamonti *et al.*, Blood 2010

Cytogenetic Abnormalities in PMF

- **del 20q**
- **del 13q**
- **Trisomy 8**
- **Trisomy 1q**
- Trisomy 9
- Monosomy 7
- t (1;7)
- del 12p
- t (1;6)

IWG-MRT: PMF and Karyotype (n= 409)

- **Patients with abnormalities: 30%**
- **Significant association with survival even after adjustment for prognostic score (p= 0.01)**
- The variable **"abnormal karyotype" increased the discriminating power** of the prognostic score, but **only in the intermediate-risk groups**.

Cervantes *et al.*, Blood 2009

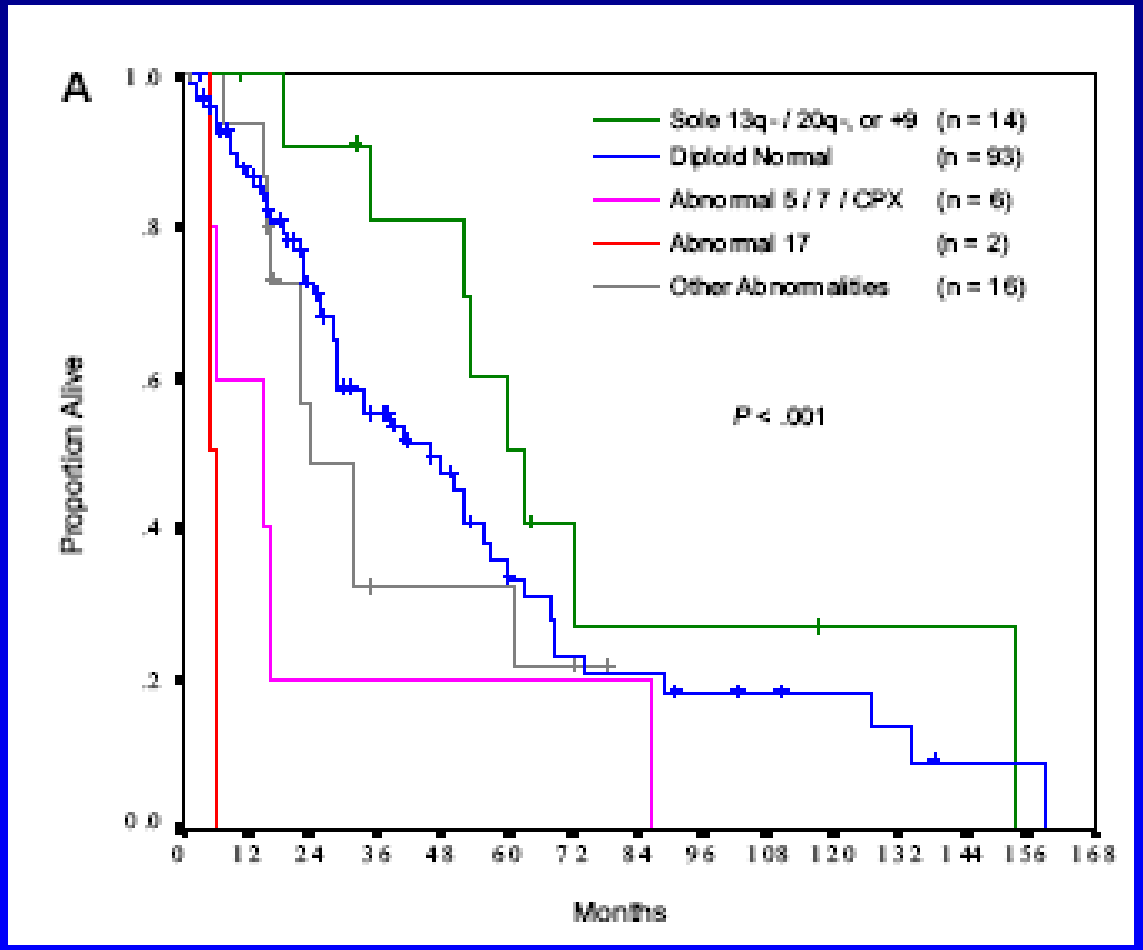
Karyotype and Prognosis in PMF

Favorable:

- 13q-, 20q-, +9
- Normal diploid

Unfavorable:

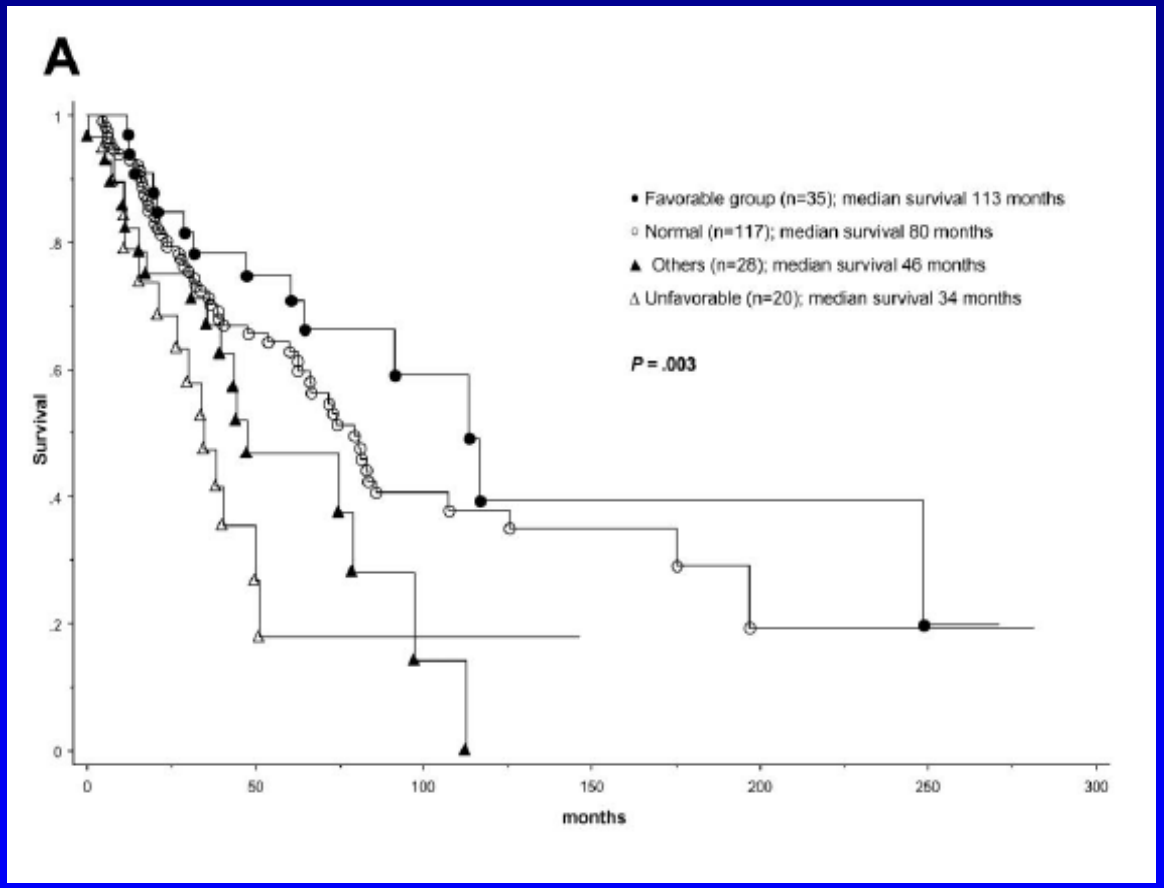
- Abnormal 5, 7 or 17
- Complex



Tam *et al.*, Blood 2009

Karyotype and Prognosis in PMF

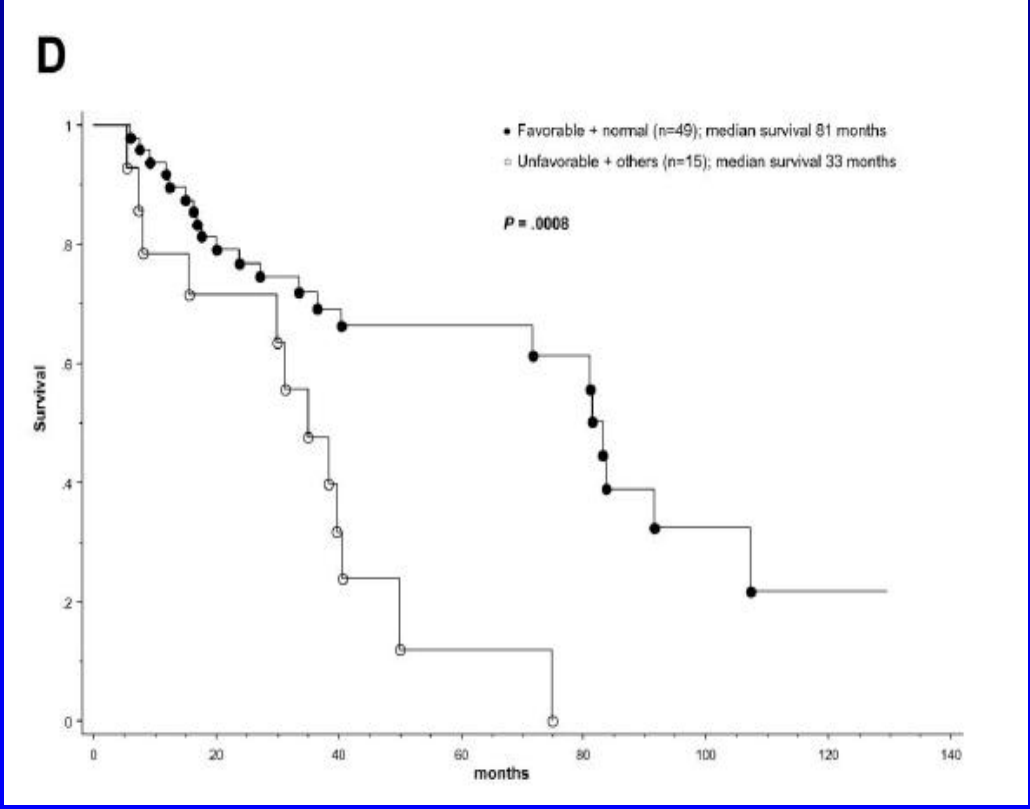
- **Favorable:**
  13q-, 20q-, +9
- **Unfavorable:**
  Complex, +8
- **Normal diploid**
- **Others**



Hussein *et al.*, Blood 2010

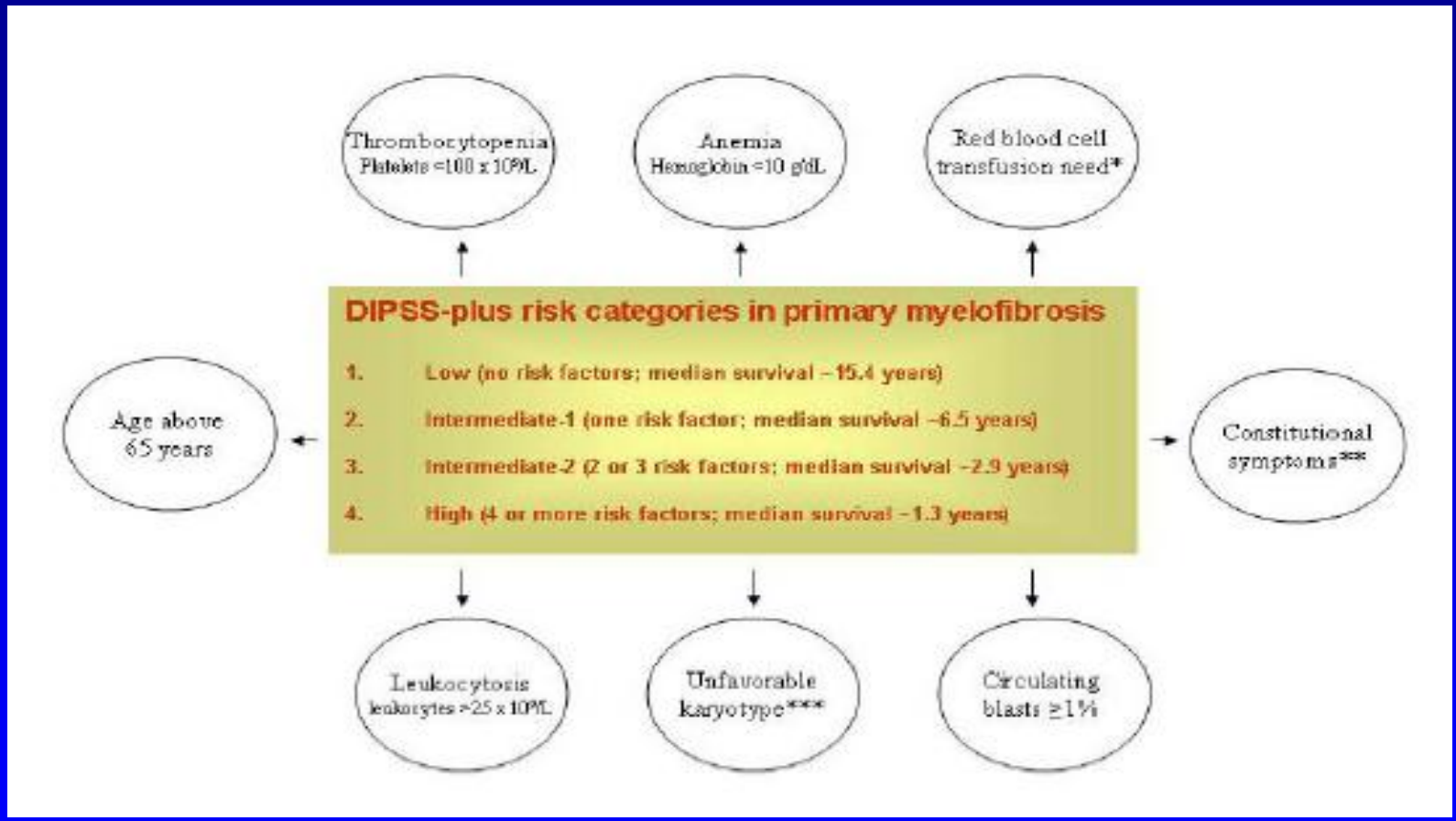
Karyotype and Prognosis in Intermediate-1 Risk PMF patients

- **Favorable + Normal**
- **Unfavorable + Others**



Hussein *et al.*, Blood 2010

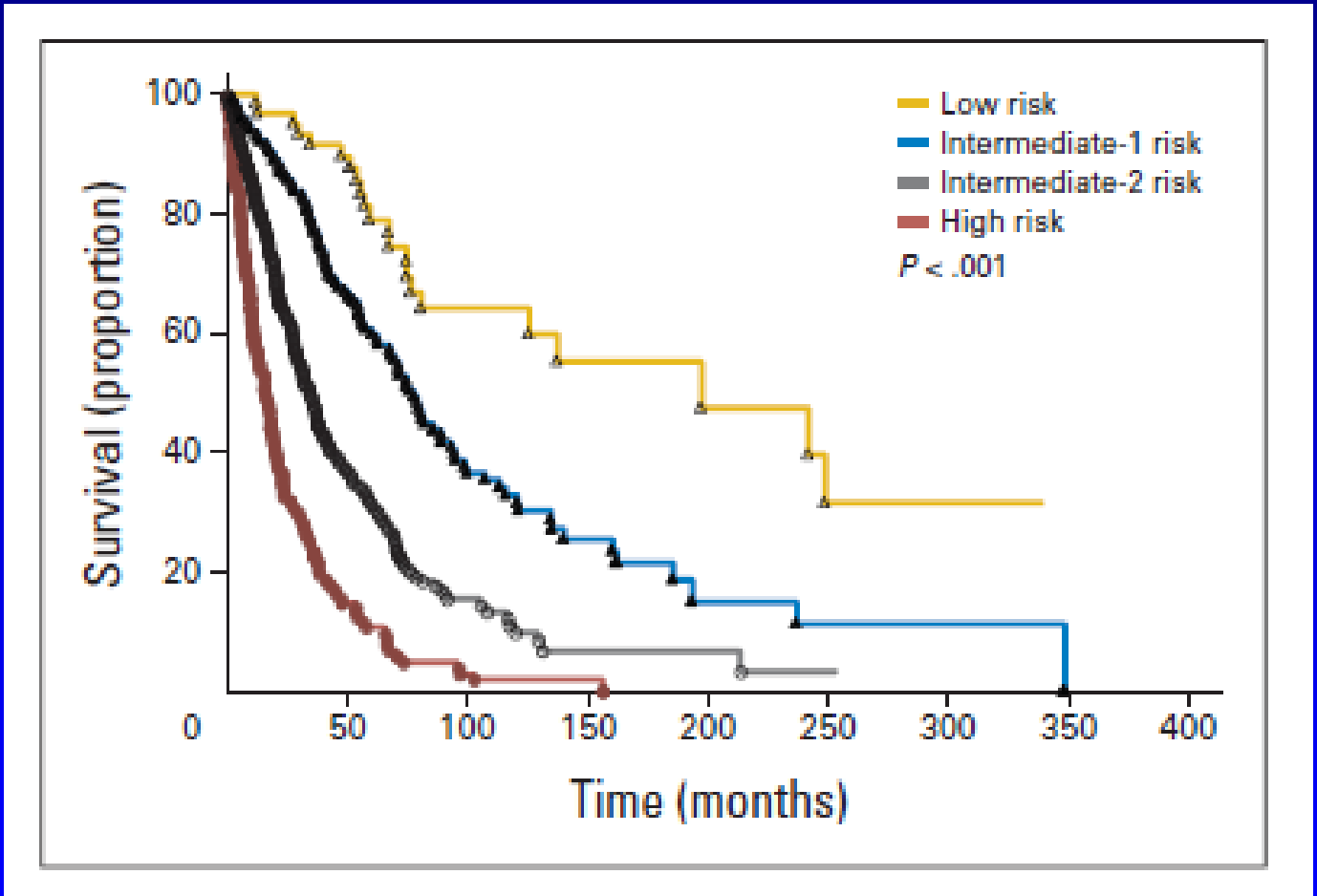
Dynamic International Prognostic Scoring System (DIPSS)-Plus for Primary Myelofibrosis



*** Complex karyotype or +8, -5/-5q-, -7/-7q, i(17q), 12p-, inv(3), 11q23 rearr.

Gangat *et al.*, JCO 2011; 29:392-397

DIPSS-Plus for Primary Myelofibrosis



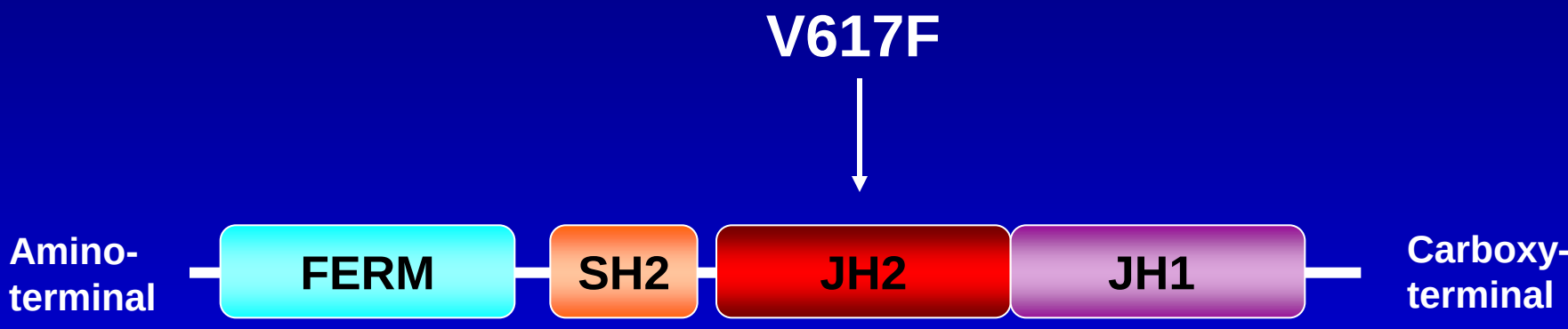
Gangat *et al.*, JCO 2011; 29:392-397

Summary of Current Prognostic Models for PMF

Variable	IPSS	DIPSS	DIPSS-plus
Age >65 y	√	√	√
Constitutional symptoms	√	√	√
Hemoglobin <10 g/dL	√	√	√
Leukocyte count >25x10^9/L	√	√	√
Circulating blasts ≥ 1%	√	√	√
Platelet count <100x10^9/L			√
RBC transfusion need			√
Unfavorable karyotype +8,-7/7q-,i(17q),inv(3), -5/5q-,12p-, 11q23 rearr.			√
	1 point each	1 point each but Hb=2	1 point each

Cervantes et al. Blood. 2009;113:2895-901.
Passamonti et al. Blood. 2010; 115:1703-8.
Gangat et al. JCO. 2010; on line Dec 13.

Mutation *JAK2* V617F in the MPNs



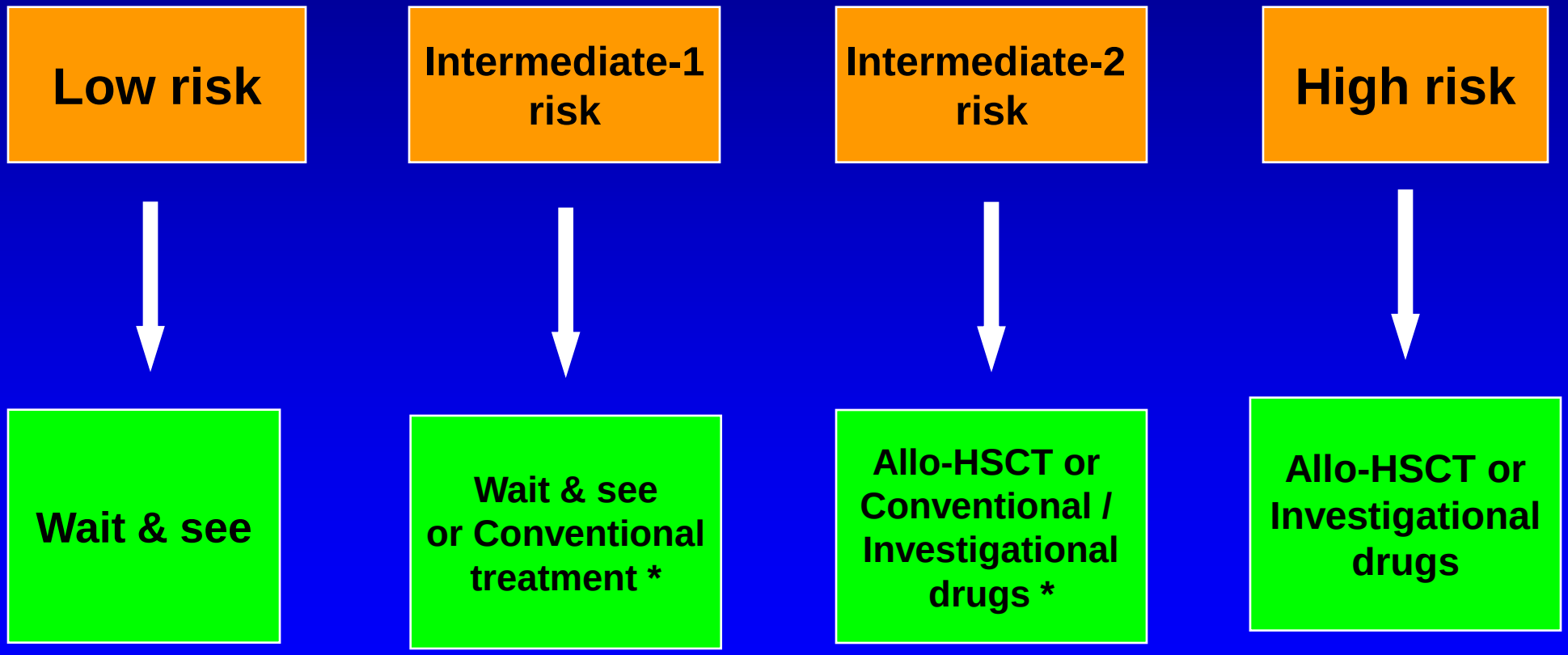
Frequency of the *JAK2* mutation	
PV	90-95%
ET	50-60%
PMF	50-60%

Prognostic Value of the *JAK2* Mutation in PMF

Author (year)	No. of patients	Prognostic influence
Tefferi (2005)	157	No
Campbell (2006)	152	Yes
Barosi (2007)	174	Yes *
Cervantes (2009)	345	No
Guglielmelli (2009)	186	Yes **

* Higher leukemic transformation rate; ** shorter survival for lower burden

Proposed Algorithm for PMF Treatment



* Check cytogenetics and transfusion dependence

* Depending on age

Conclusions

- **Median survival of PMF patients is higher than 5.5 years but there is a wide heterogeneity.**
- **Main prognostic factors are age > 65 years, constitutional symptoms, Hb < 10 g/dL, leukocytosis > 25 x10^9/L, and blood blasts ≥ 1%; certain karyotypic abnormalities, transfusion need and thrombocytopenia also contribute to prognosis.**
- **Based on the above factors it is possible to identify four risk groups at diagnosis and during the disease evolution.**
- **These risk groups are of help in treatment-decision making.**


+100
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