

Revised International Prognostic Scoring System (IPSS-R):  
Developed by the International Working Group for Prognosis  
in MDS (IWG-PM)

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for the IWG-PM

# MDS Classifications

- 1997 IPSS/IMRAW (FAB): 816 pts/7 DBs
  - Marrow blasts, cytogenetics, cytopenias
- 2001 WHO classification
  - Dysplastic subgroups, RAEB-1,2, del(5q)
- 2007 WPSS: 1165 pts/3 DBs
  - WHO subgroups, IPSS cytogenetics, RBC Txns
- 2001-2011 New features described as possible additional prognostic factors
- New cytogenetic classification: 2900 pts/4 DBs
- 2011 IWG-PM Refined consensus system (IPSS-R)
  - 7012 pts/18 DBs

# IWG-PM: Aims for Refining IPSS

- Determine impact of newer features for prognostic power
- Incorporate larger cytogenetic subgroups & Re-assess their prognostic impact
- Analyze depth of cytopenias
- Provide better prognostic ability
- Maintain continuity, feasibility, flexibility

# IWG-PM

Tuechler, Haase, Schanz, Greenberg  
Cytogenetic Committee, PIs confirm DBs

- Vetted DBs from 18 institutions → Combined DB
  - 1<sup>0</sup> untreated, accuracy, completeness, cytogenetics, outcomes
- Further assessed cytogenetics: standard ISCN
  - Cytogenetic Committee review
- Data review, statistical weighting for predictive power
- Data analysis
- Final IPSS-R model generated

# IWG-PM: Inclusion criteria

- Primary MDS (FAB or WHO)
  - Marrow blasts  $\leq 30\%$ ; PB blasts  $\leq 19\%$
  - WBC  $\leq 12,000/\text{mm}^3$  (ANC  $\leq 8,000$ )
  - $\geq 2$  months stable disease
- Marrow blasts, Cytogenetics, Hb, ANC, Platelet levels documented
- No disease-altering therapy during chronic phase
- Valid survival data
- Age  $\geq 16\text{yo}$

# IWG-PM Database PIs

12 countries/18 DBs, n=7012

Austria- Innsbruck Vienna Linz	Stauder Pfeilstoecker Krieger	Japan	Miyazaki
Brazil	Magalhaes	Netherlands	van de Loosdrecht
Czech Rep	Cermak	Scotland	Bowen, Tauro
France	Fenaux	Spain	Sanz, Sole, Vallespi
Germany- Dusseldorf Freiburg Goettingen	Germing Luebbert Haase	USA- MD Anderson Cleveland Clinic	Garcia-Manero Sekeres
Italy- Alessandria Pavia	Levis Cazzola Malcovati	IMRAW	Greenberg Bennett

# Combined DB--Variables (1)

- 7012 pts from 18 DBs
- Age 71yo (median), M:F 1.5:1
- Followup time 3.9yr, median
- FAB 7000 pts; WHO 5504 pts (79%);  
WPSS 2325 pts (33%)
  - RAEBT 6%, CMML 9%, 5q- 4%
- Ferritin 43%; RBC Txn Dept 13% (32% w/ data)
- BM fibrosis 19%, LDH 61%, B2M 13%,  
PS-ECOG 36%

## Combined DB--Variables (2)

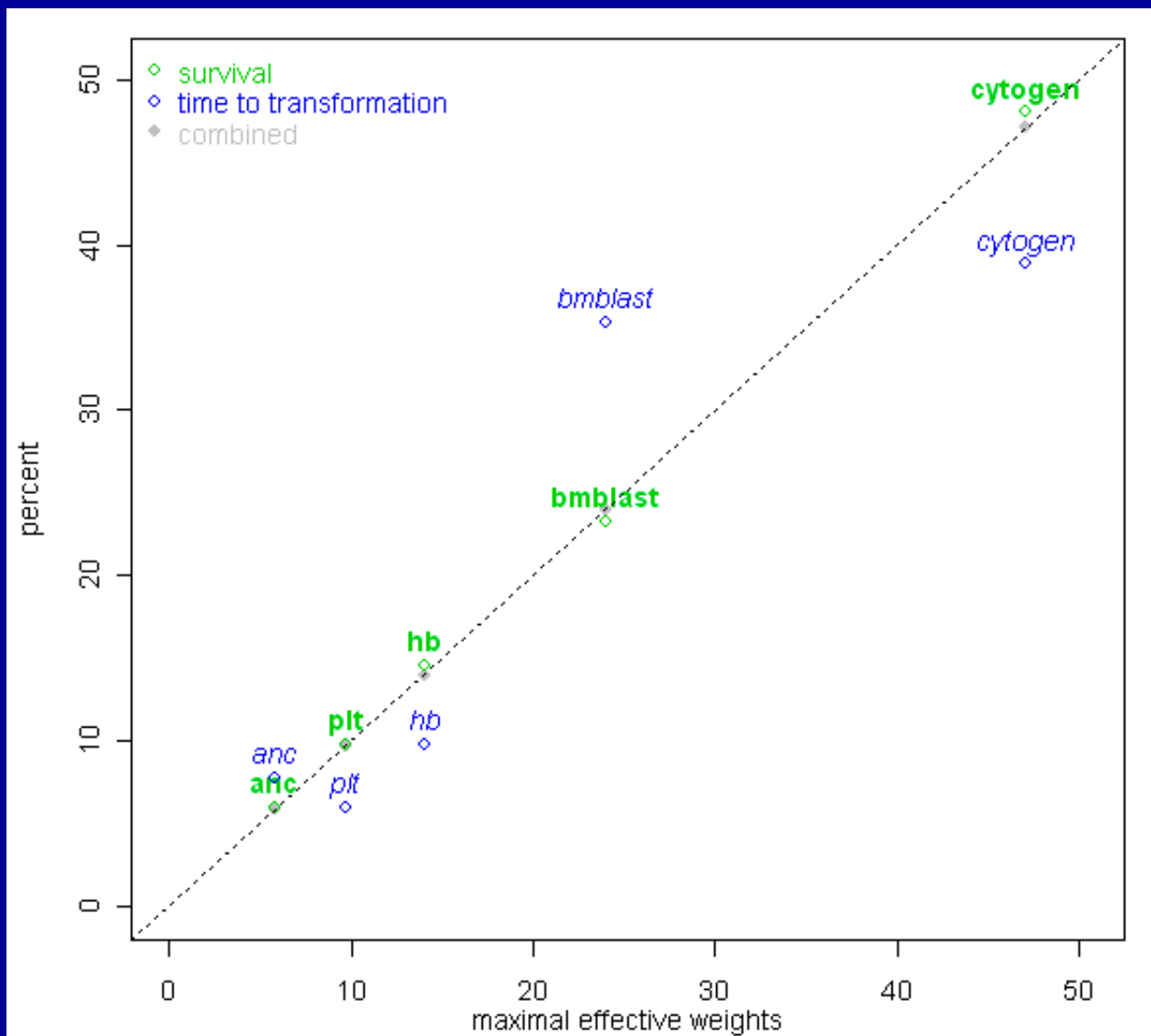
- Cytogenetics, n=7001
  - IPSS Good/Int/Poor 75/13/12% ('97: 74/15/11)
  - *IPSS-R: V Good/Good/Int/Poor/V Poor: 4/72/13/4/7%*
- IPSS categories, n=7008
  - Low/Int1/Int2/High 37/40/16/7%  
(*'97: 33/38/22/7*)
- WPSS categories, n=2325
  - 22/32/20/20/4%  
(*'07: 23/28/19/23/7*)

# IPPS-R: Cytogenetic Prognostic Subgroups

- Very Good: del(11q),-Y
- Good:NI, del(20q), del(5q) alone and double, del(12p)
- Intermediate: +8, 7q-, i(17q),+19,+21, any other single or double, independent clones
- Poor: der(3)q21/q26,-7, double including 7q-, Complex (3 abnormalities)
- Very Poor: Complex (>3 abnormalities)

*Schanz et al, J Clin Oncol, in press*

# IPSS-R: Statistical Weights of Predictive Variables



## IPSS-R for MDS: Prognostic Score Values\*

	0	1	1.5	1.5	2.5	3.5	5
<b>Cyto</b>	Very Good		Good		Int	Poor	Very Poor
<b>Blasts</b>	<5%			5-10%	11-30%		
<b>Hb</b>	≥10			<10			
<b>Plt</b>	≥100		<100				
<b>ANC</b>	≥0.8	<0.8					

\*Regression analysis for survival and AML evolution

# Prognostic Risk Groups/Scores\*

1. Very Low: 0 - 2
2. Good: >2 - 3.5
3. Intermediate: >3.5 - 5
4. High: >5 - 6
5. Very High: >6

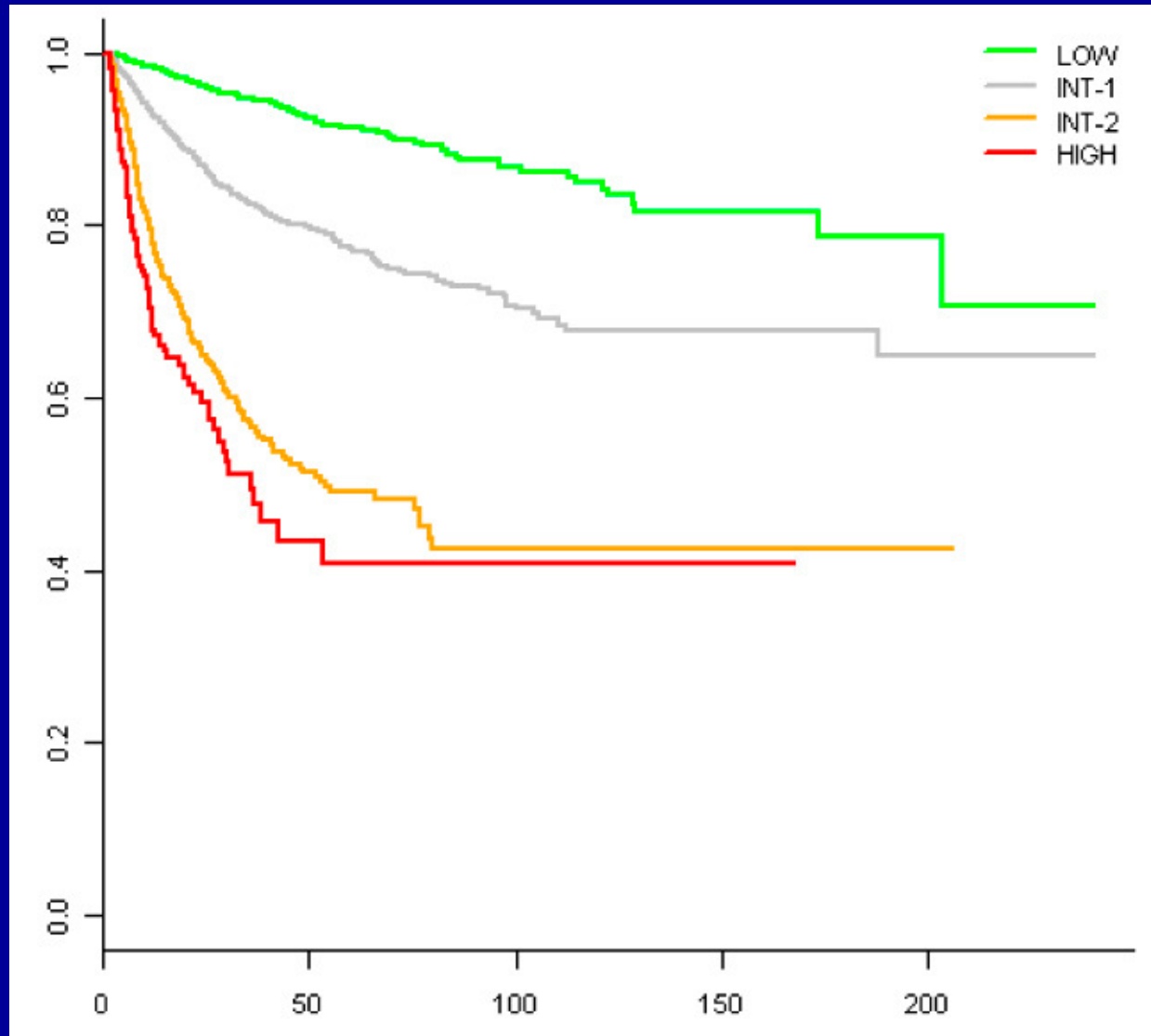
\*Values for 70yo patient

For consideration of age:

(age in yrs - 70) x 0.04, add result to sum of other variables

# IPSS Freedom from AML Transformation

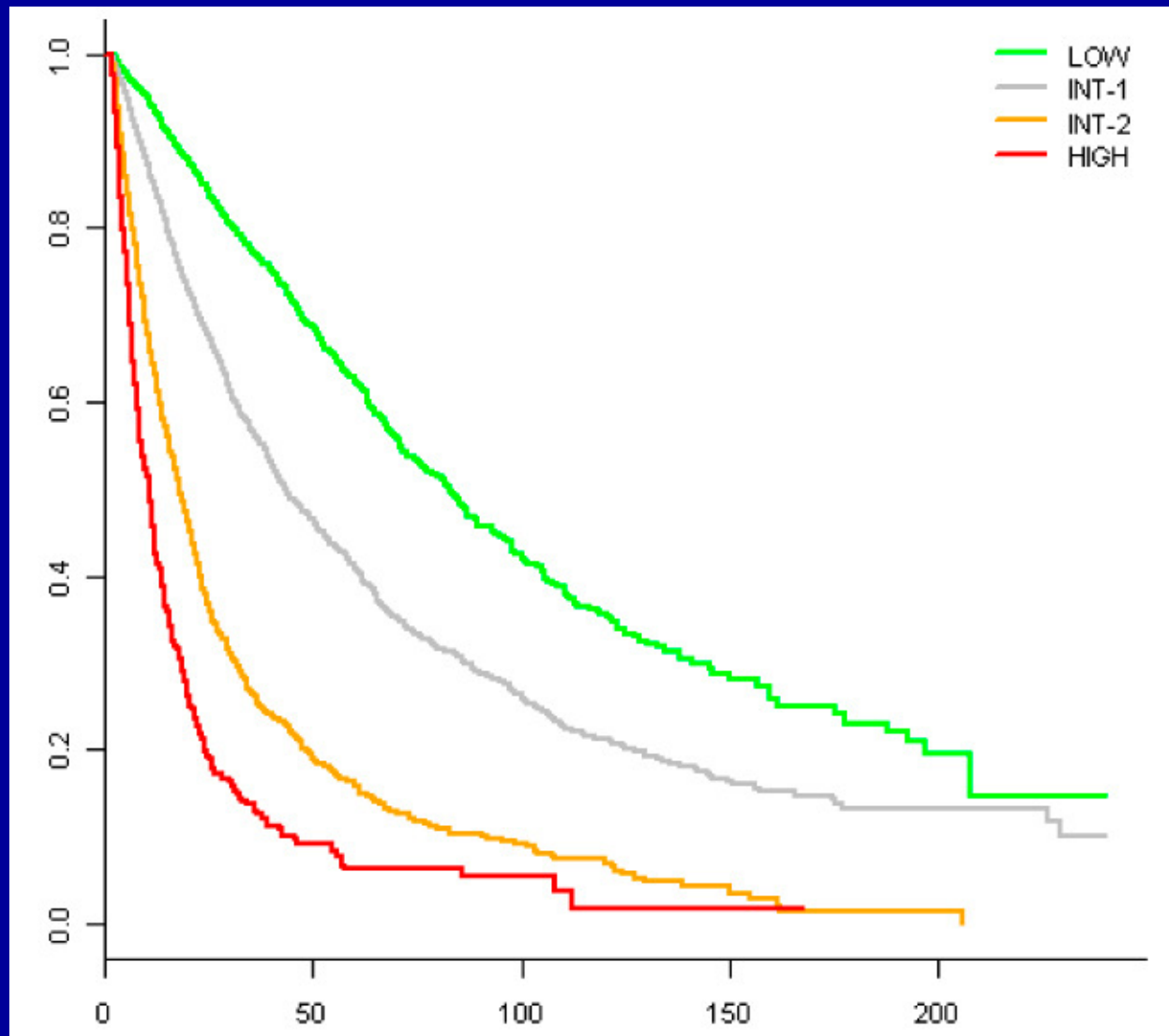
n=7008



Dxy 0.48

Months

# IPSS Survival, n=7008

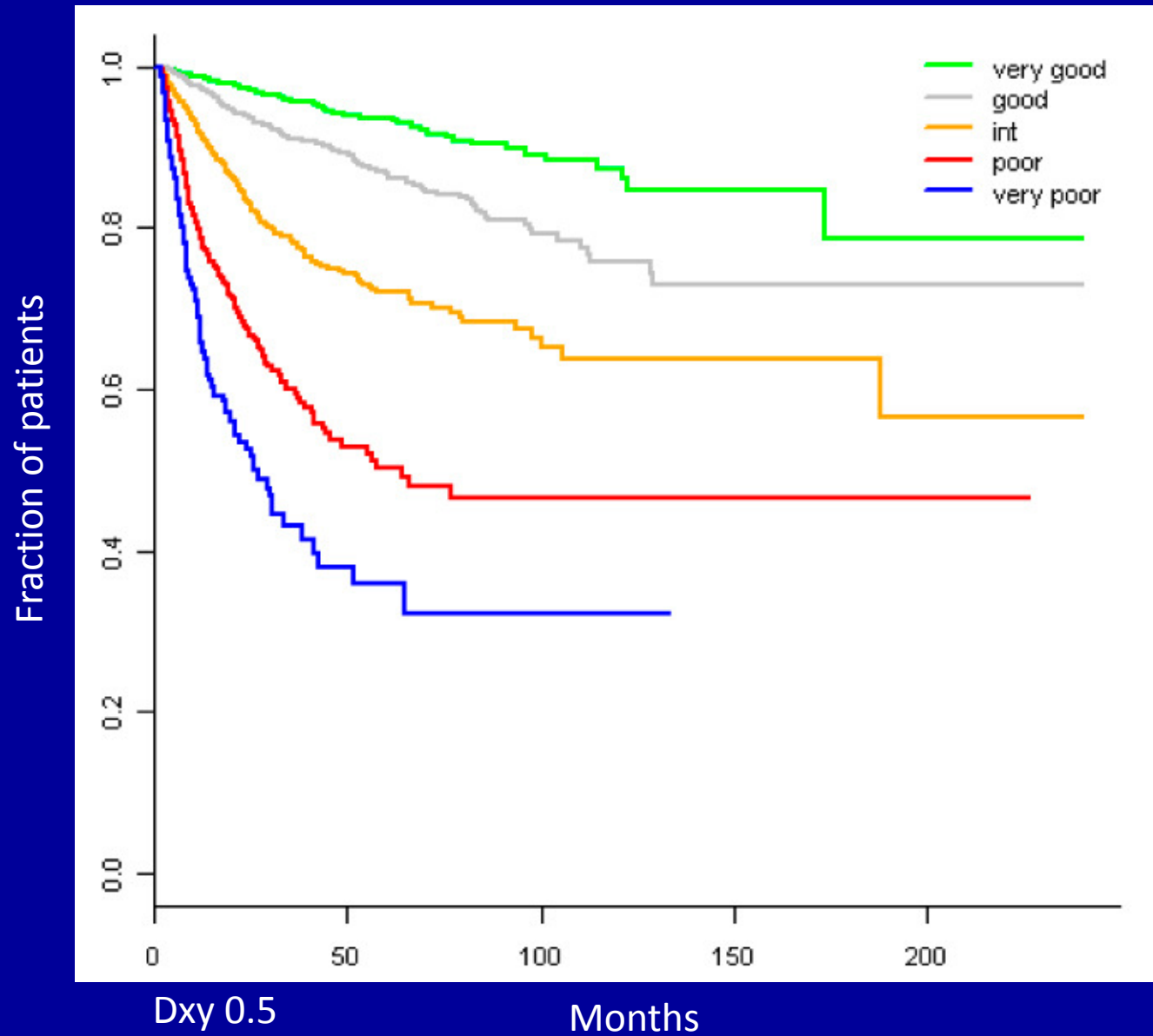


Dxy 0.37

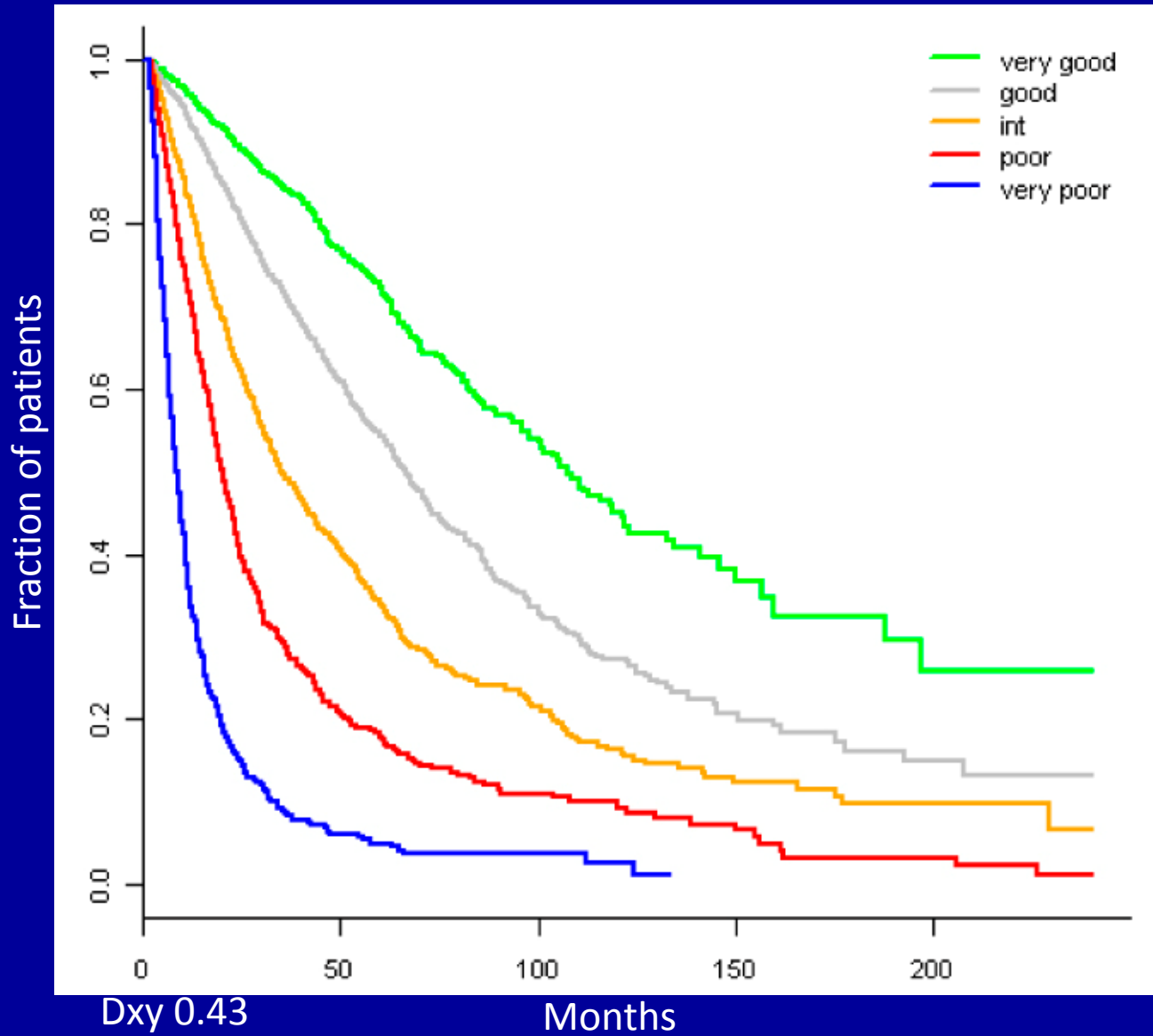
Months

# IPSS-R Freedom from AML Transformation

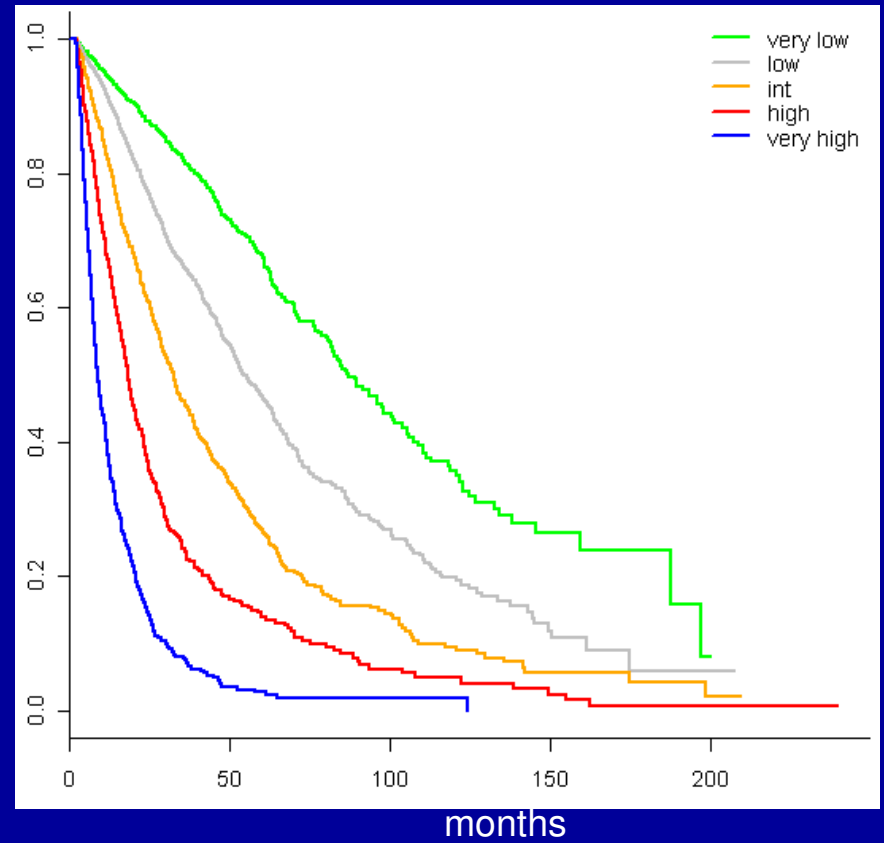
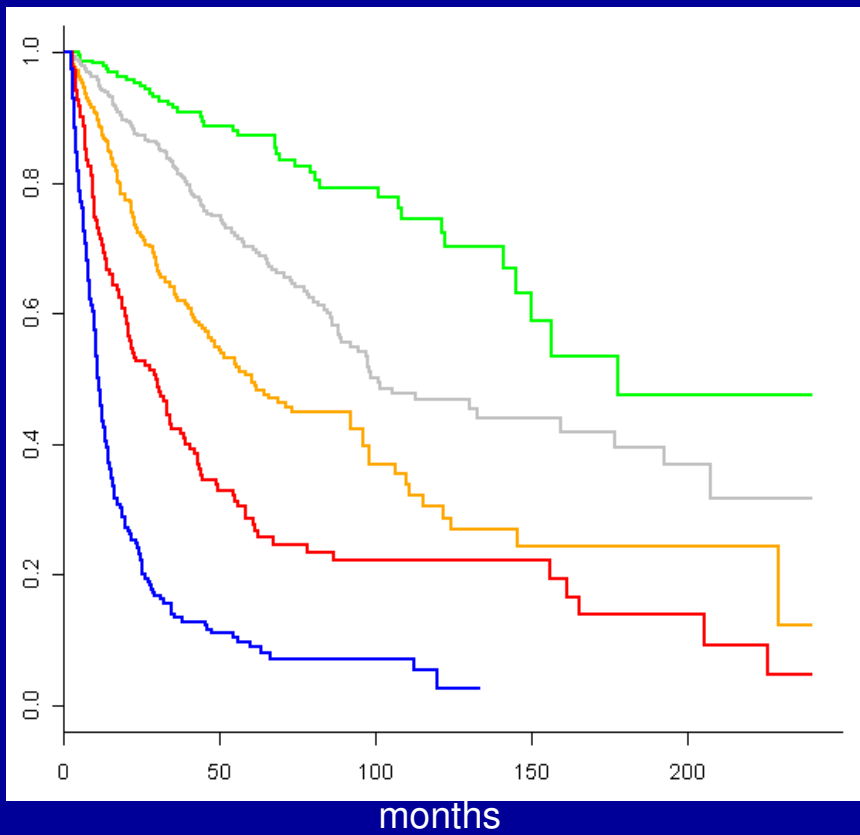
n=7012



# IPSS-R Survival, n=7012



# IPSS-R: Survival $\leq 60$ vs $>60$ yo



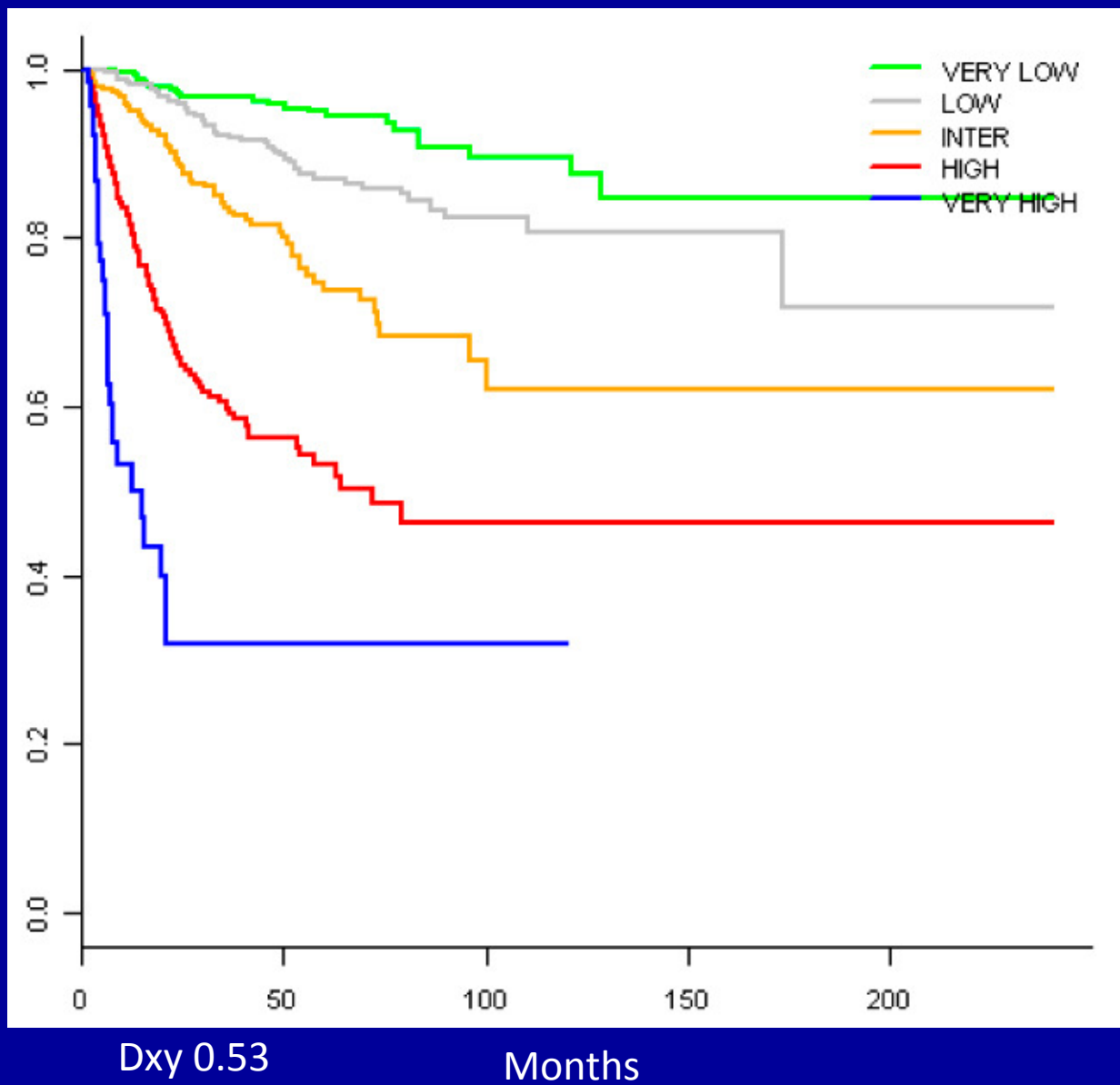
# IPSS-R: Prognostic Subgroup Clinical Outcomes\*

	1 Very Low	2 Good	3 Inter- mediate	4 Poor	5 Very High
OS	8.7	5.3	3.0	1.6	0.8
AML, 25%	NR	10.7	4.0	1.4	0.8

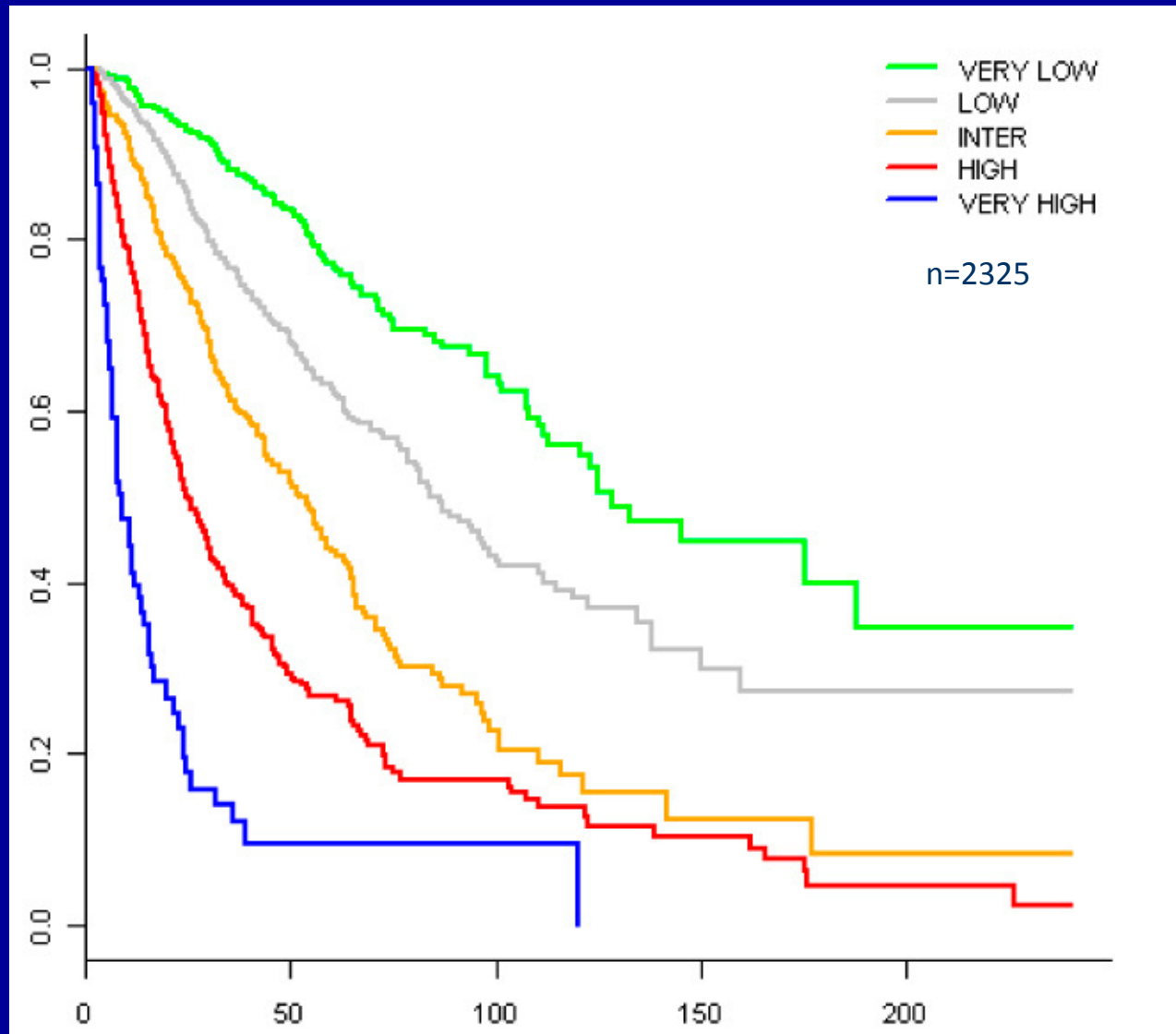
\*Medians, years

# WPSS-R Freedom from AML Transformation

n=2325



# WPSS-R Survival, n=2325



Dxy 0.42

Months

# IPSS-R: Additive Prognostic Variables\*

	Total cases	Survival	AML
Age	100%	+++	-
PS/ECOG	36%	++	-
Ferritin	43%	+	-
Fibrosis	19%	-	-
LDH	59%	+	-
B2M	15%	(++)	-

\*Based on  $p < .05$  & gain in Dxy concordance coefficient/predictive value  
(Cox proportional hazard models)

# IPSS-R, WPSS-R: Advances Beyond the IPSS & WPSS

- Added refined cytogenetic subgroups (*16 vs 7*) & prognostic categories (*5 vs 3*)
- Analyzed depth of cytopenias
- Improved predictive power w/ more precise prognostic subgroups (*5 vs 4*)
- Clear impact of *age* and additional predictive features for survival
  - PS, ferritin, LDH

# IWG-PM Directions

- Morphologic review of 'low blast' dysplasia
  - Further evaluation of WPSS-R
- Web-based calculator tool
- Resource for the field
- IPSS-R/Molecular-1,-2
  - Impact of molecular lesions on the IPSS-R
- Dynamic IPSS-R
- IWG-PM for Treated and 2<sup>0</sup> MDS pts