



Epidemiology of MDS

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HEALTH SCIENCES CENTRE

when it matters
MOST



Definition: Epidemiology

“The study of the distribution of diseases in populations and of factors that influence the occurrence of disease”

- Data sources: death certificates, disease registries, population censuses, surveys
 - **Mortality**
 - **Incidence**
 - **Prevalence**



Objectives

- What is the incidence and prevalence of MDS in general population?
- Review known risk factors for MDS
- Compare differences in MDS between Caucasian and Asian populations and in those aged < 50
- Discuss the prevalence of unexplained anemia in the elderly
- Present Sunnybrook MDS prevalence data from investigations of unexplained low blood counts



Epidemiology of MDS: General Comments

- **MDS complex and varied group of malignant stem cell disorders**
- **Until recently, poorly documented incidence and prevalence data**
- **Estimates ranged from 1500-15,000 new cases per year – increasing????**
 - **Aging population**
 - **Better diagnostic capabilities**
 - **Improved recognition**
 - **More therapeutic options**
 - **More survivors of cancer**



Risk Factors for MDS

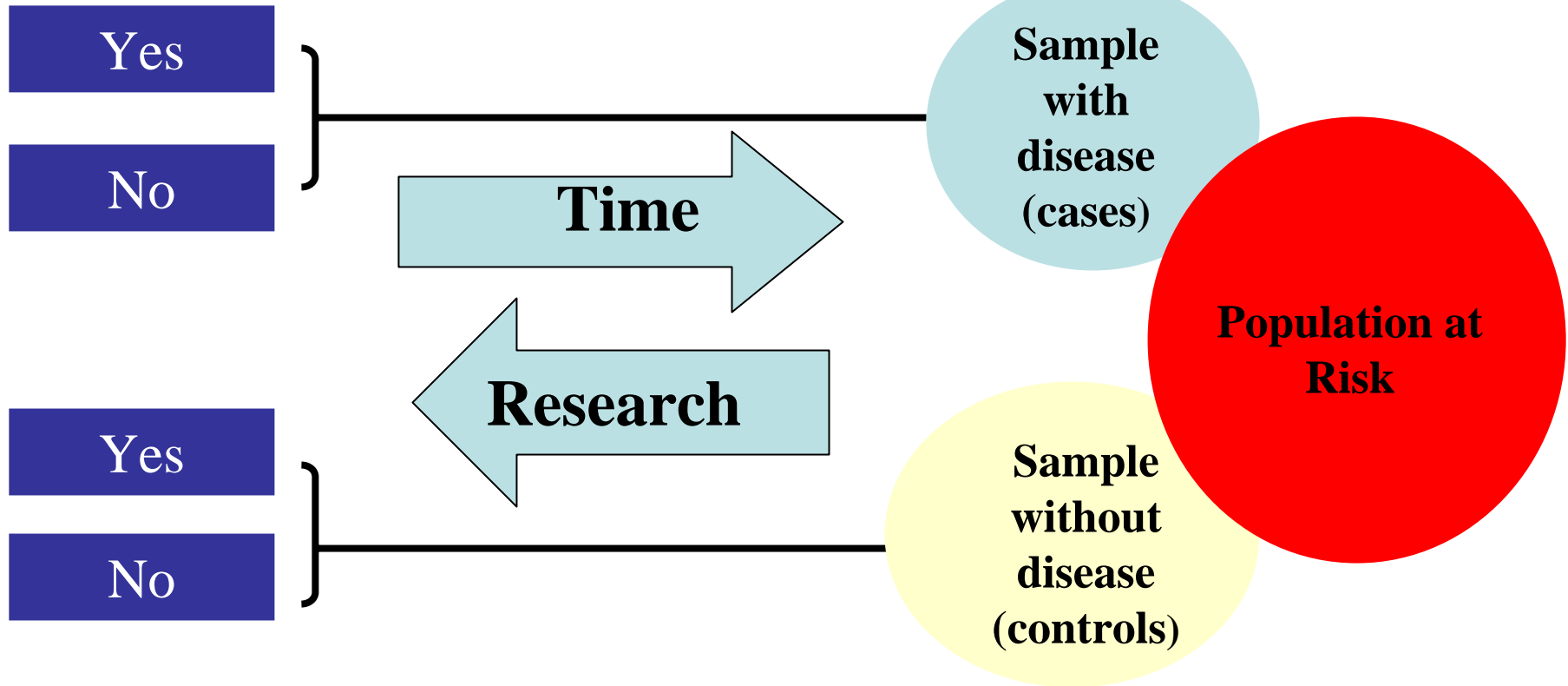
- 80% Unknown
- Age
- Gender
- DNA damaging drugs
 - **Chemotherapy**
 - **Environmental/occupational**
 - **Smoking**
 - **Ionizing Radiation**
- Rare-Inherited abnormalities
 - **Fanconi's anemia, congenital MDS**



Case control diagram

Smoking

Myelodysplasia





Epidemiology of MDS: case control study at MDACC n=354 patients

Risk Factor:	Odds Ratio:
Smoking	1.65
Family history	1.92
Agricultural chemicals	4.55
Organic solvents	2.05
Smoking + chemical	3.22
Wine drinkers	0.54

Strom S. et al. Leukemia 2005;19(11):1912-8.



Occupational Groups At risk for MDS

- Painters
- Plant and machine operators
- Coal miners
- Embalmers
- Garage and transport workers
- Shoe workers
- Hair dressers and cosmetologists
- Sea men on tankers
- Research science technicians
- Farmers



Diet and MDS

- Hypothesis:
 - Dietary intake and secondary production of phenol (and hydroquinone)
 - People who eat a high-meat diet have increased production of phenol
 - Arbutin rich food (wheat)

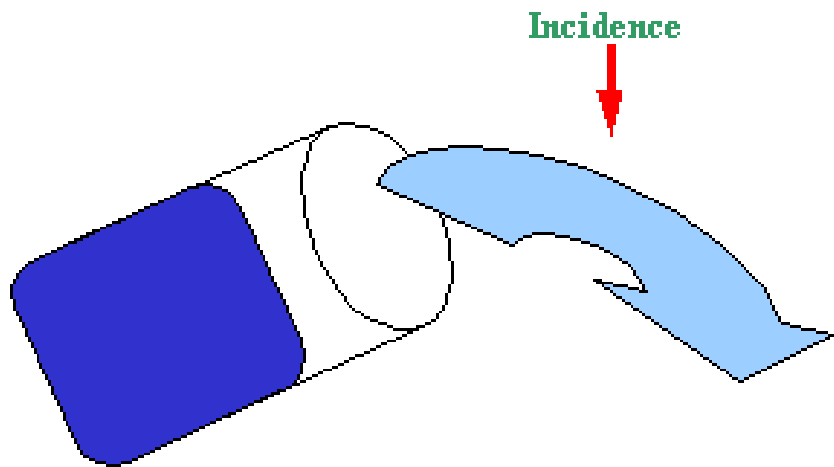


Summary: Cause of MDS

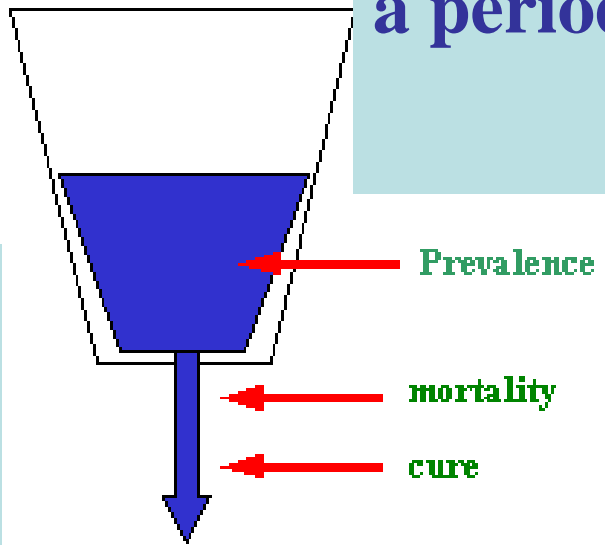
- De novo: combination of genetic susceptibility, environment, occupation, smoking, diet?
- Therapy related: DNA damaging chemotherapy or radiation
- A lot more needs to be learned!



Incidence - the number of new occurrences of a condition (or disease) in a population over a period of time



Prevalence - the measure of a condition in a population at a given point in time



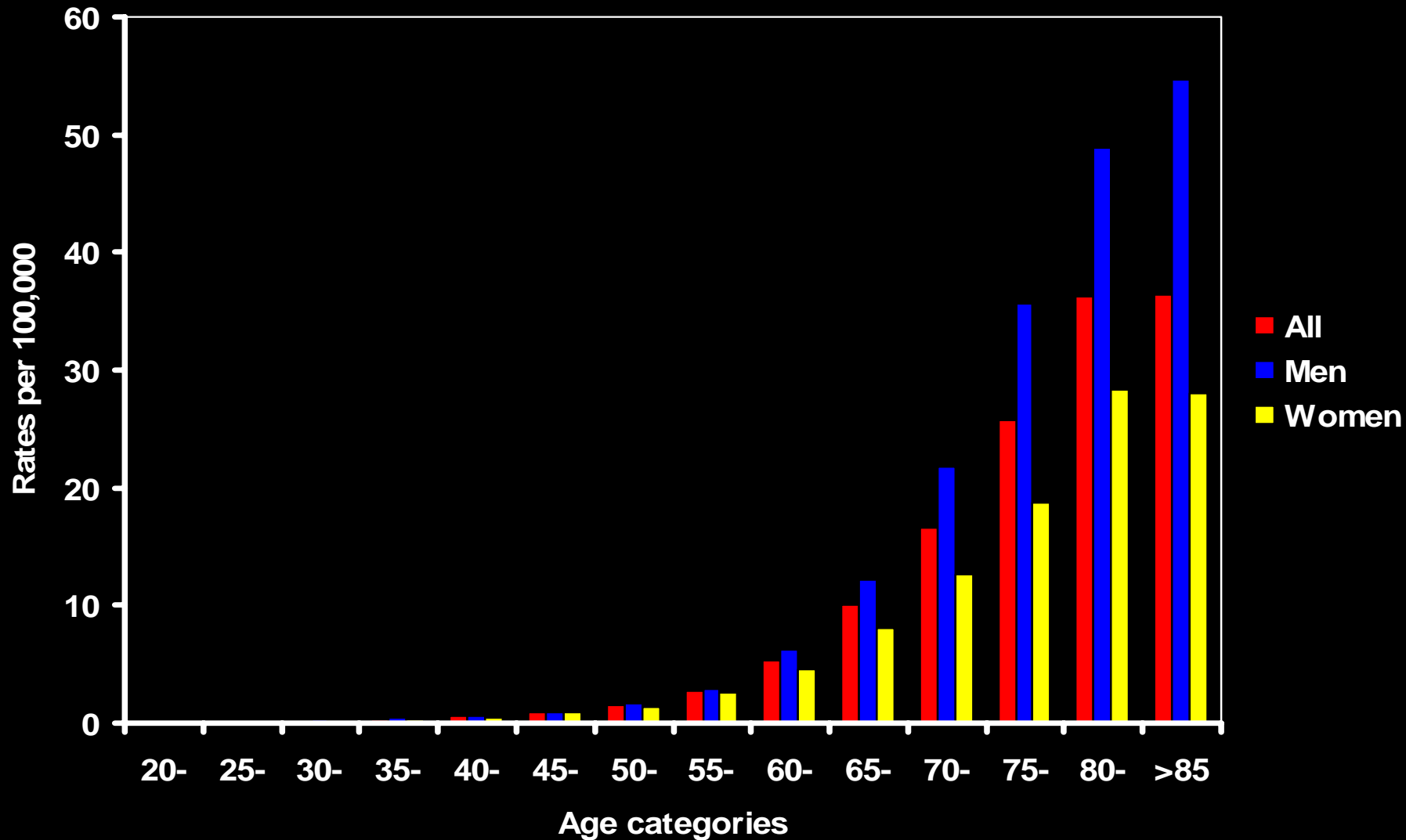


MDS Incidence: SEER database 2001-2003

- 7131 cases reported
- Incidence: 3.4/100,000
 - 4.5/100,00 in men; 2.7/100,000 in women
- Risk of MDS increased with age
- Median age at diagnosis: 76
- Varied by sex and race
- Estimated 10,300 cases were diagnosed in US in 2003

Ma X. et al. Cancer 2007;109:1536-42

Age-Specific Incidence Rates of MDS in the US 2001-2003: SEER database





Incidence Rates by Sex and Race

Variable	All	Men	Women
All races	3.4	4.5	2.7
White	3.5	4.6	2.7
Black	3	3.5	2.7
American Indian/Alaska Native	1.3	1.8	1
Asian or Pacific Islander	2.6	3.2	2.2

Registry Incidence* data by age


Registry	50-69	70-74	75-79	80-84
SEER 2007	4.1	16.6	25.7	36.2
Dusseldorf 2007	4.9	24.5		31.3
UK 1987	4.1	12.7	23.4	42.5

* *Denotes per 100,000*



SEER Age adjusted incidence rates in hematology 65+

<u>Disease</u>	<u>Rate/100,000</u>
AML	16.7
CLL	22
Myeloma	29
Hodgkin's	3.9
MDS	16-36



Differences in clinical features between Japanese and German Patients with RA in MDS

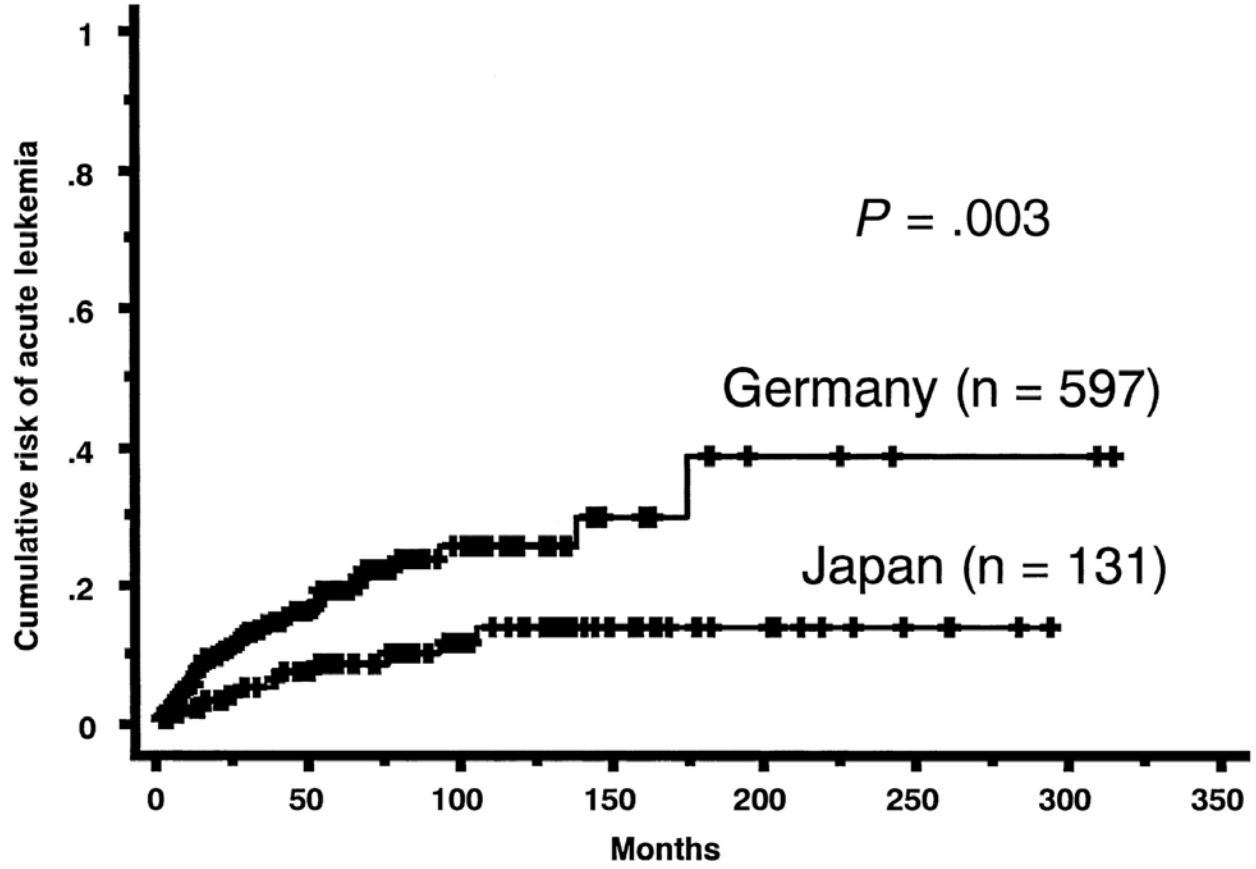
- Study compared clinical features and prognostic factors between 131 Japanese and 597 German patients
- Compared overall and disease related survival between both groups

Matsuda A. et al. Blood 2005;106:2633-2640

	Japan (n=131)	Germany (n= 597)	P
Age	57 (12-88)	71 (7-93)	<.001
2-3 reduced counts	68%	39%	<.001
Plt count	38 (4-246)	127(13-390)	.026
Abn. Chromosomes	29%	53%	<.001
Del 5q	8%	20%	
Low / Int-1	20% / 72%	48% / 45%	
Median Survival	175 mos	40 mos	<.001
IPSS prognostic	no	yes	

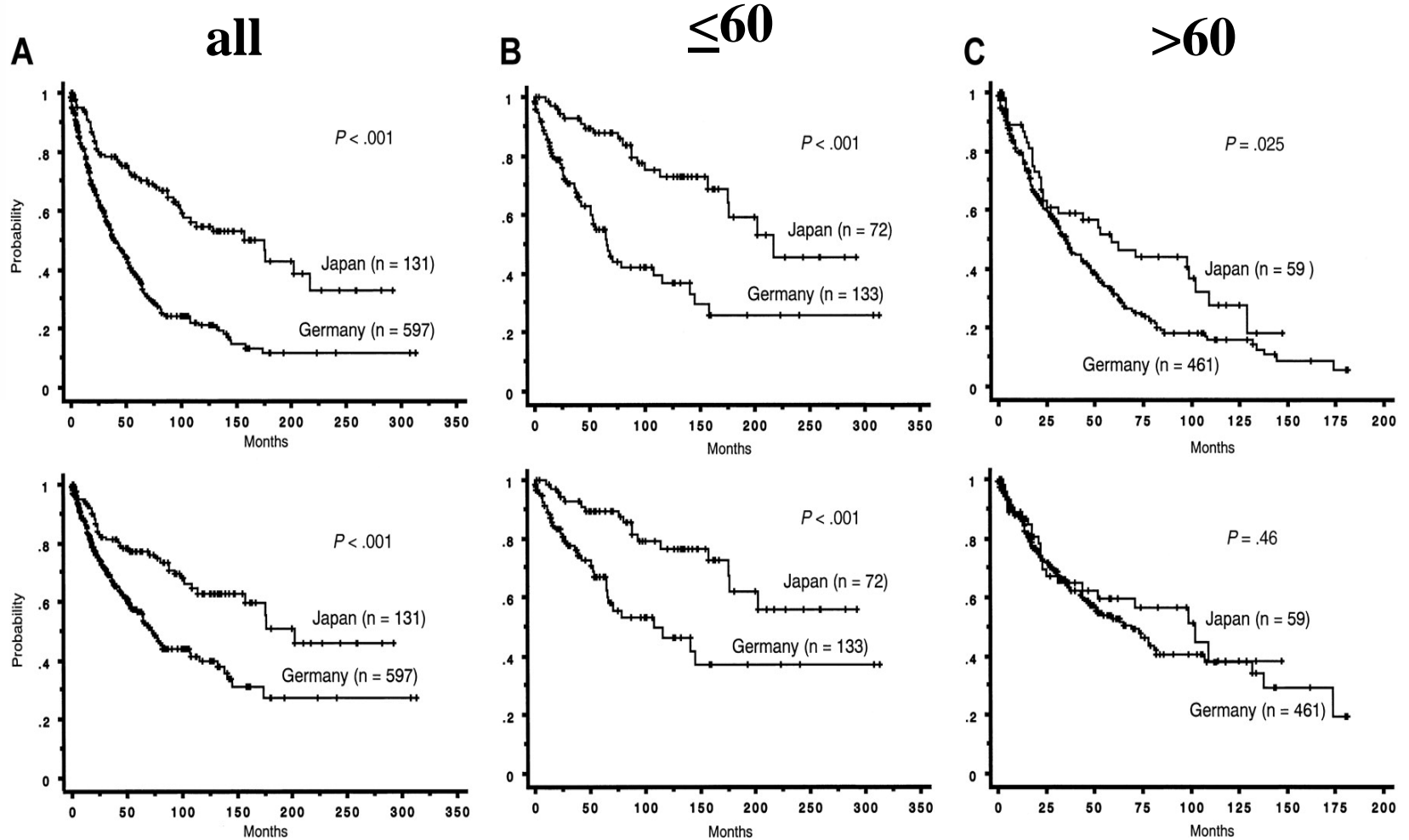
Matsuda A. et al. Blood 2005;106:2633-2640

Figure 1. Cumulative risk of acute leukemia evolution of patients with FAB-RA



Matsuda, A. et al. Blood 2005;106:2633-2640

Figure 2. Cumulative survival of patients with FAB-RA



Matsuda, A. et al. Blood 2005;106:2633-2640



MDS in young patients

2728 MDS patients analyzed (232 age < 50)

- 8% aged < 50 at diagnosis
- Baseline blood values, classification and risk scores identical
 - More common in females
 - More deaths do to MDS (67 vs 45%)
 - Overall survival better
 - 20 year OS 80% in low risk MDS



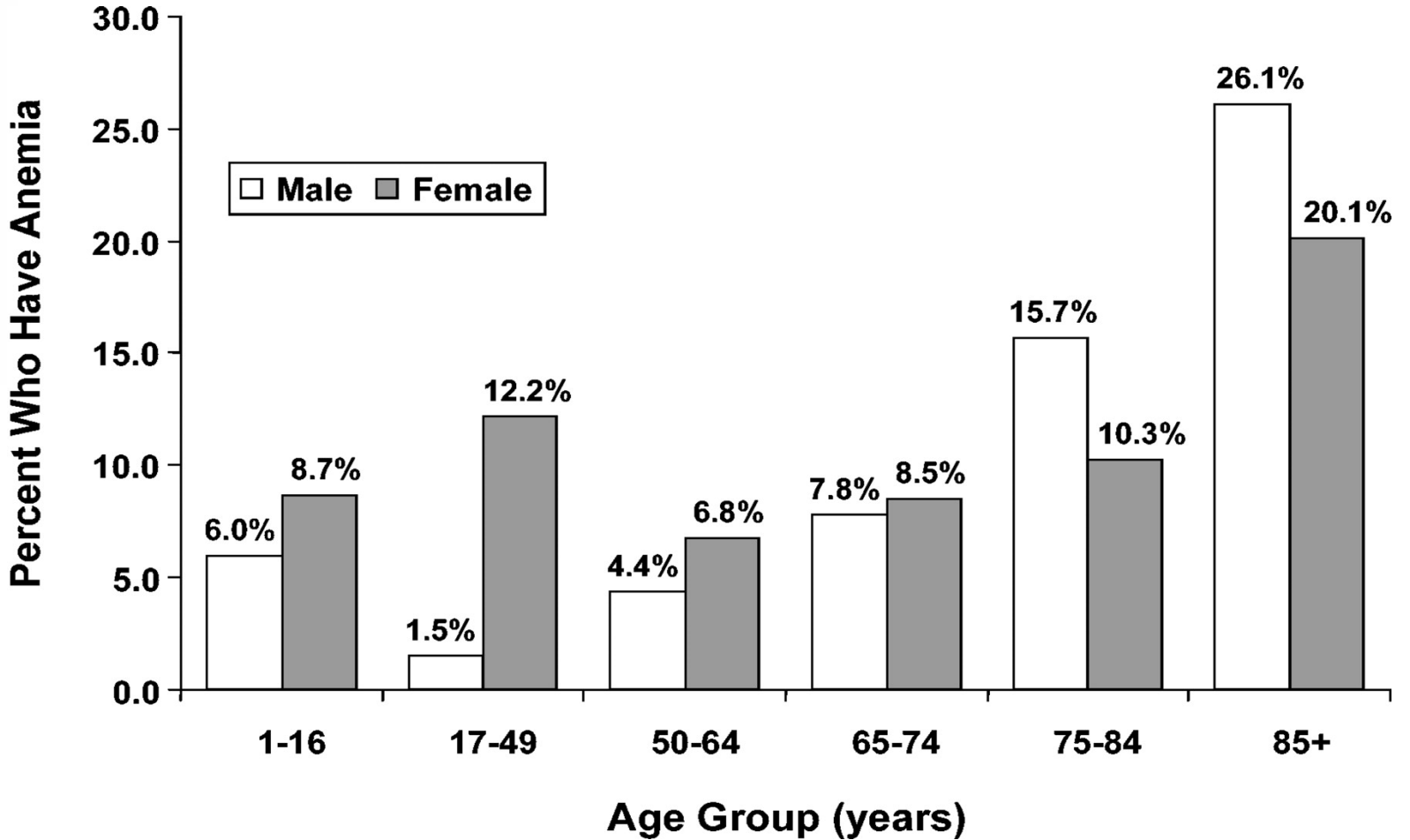
What is MDS Prevalence?



MDS Prevalence: NHANES survey III

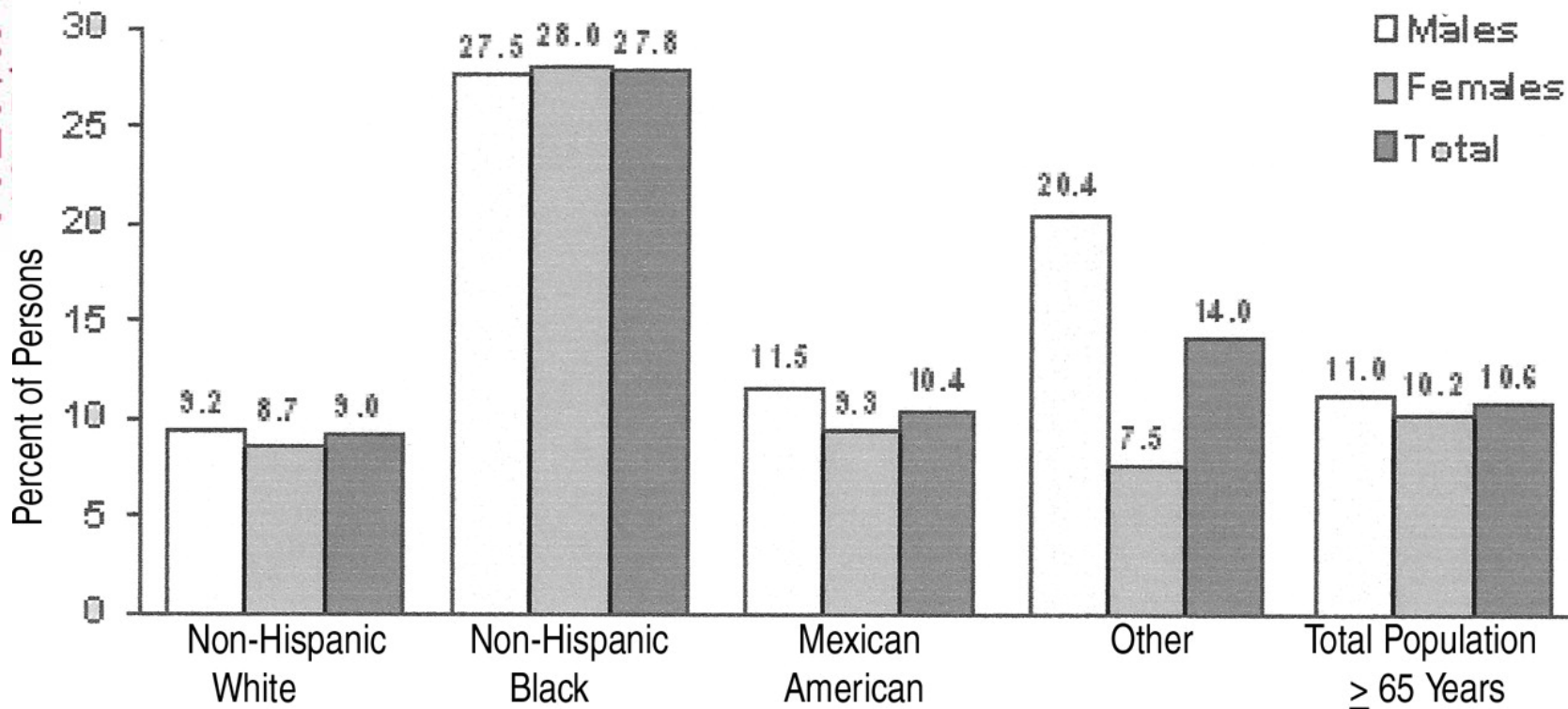
- **39, 695 non-institutionalized US population (1988-1994)**
- **4199 interviewed people 65 + yrs had complete blood count**
- **Results:**
 - **Prevalence of anemia 10.6%**

Figure 1. Percentage of persons considered anemic according to age and sex



Guralnik, J. M. et al. Blood 2004;104:2263-2268

Figure 1. Percentage of persons age 65 and older who are anemic, by race/ethnicity and sex



Guralnik, J. M. et al. Hematology 2005;2005:528-532

US distribution of types of anemia in persons > 65 in 2002: NHANES III

Type of Anemia	%	Est. Pop.
Blood Loss/Nutrition	34	965,544
Iron deficiency and iron with folate and/or B12 deficiency	20	561,936
Folate and or B12 deficiencies	15	403,608
Chronic Disease (EPO deficiency)	32	904,136
Chronic kidney disease (CKD)	8	229,686
Anemia of chronic disease (ACD)	20	554,281
CKD and ACD	4	120,169
Unexplained Anemia	34	945,195



Unexplained Anemia in NHANES III.....

- Of the 1/3 with unexplained anemia, 17% had associated one or more additional features suspicious for MDS
- Do 5.8% of the 2.8 million anemic adults > 65 in US have MDS (n=160,000)?



Objective

- **Primary:** Better refine the estimate of MDS prevalence in patients with anemia or reduced blood counts using the gold standard - bone marrow
- **Secondary:** Identify any pre-test characteristics predictive of MDS



Methods

- **4 year retrospective survey of all bone marrows reviewed at Sunnybrook for the investigation of reduced blood counts**
- **Excluded outside referrals**
- **Reviewed electronic charts for potential risk factors that might contribute to the reduced blood counts**



Methods Continued...

- **Characteristics of the peripheral blood values at time of BM recorded**
- **BM graded as:**
 - **confirmed MDS**
 - **suspected MDS**
 - **non-diagnostic**
 - **normal**
 - **other**



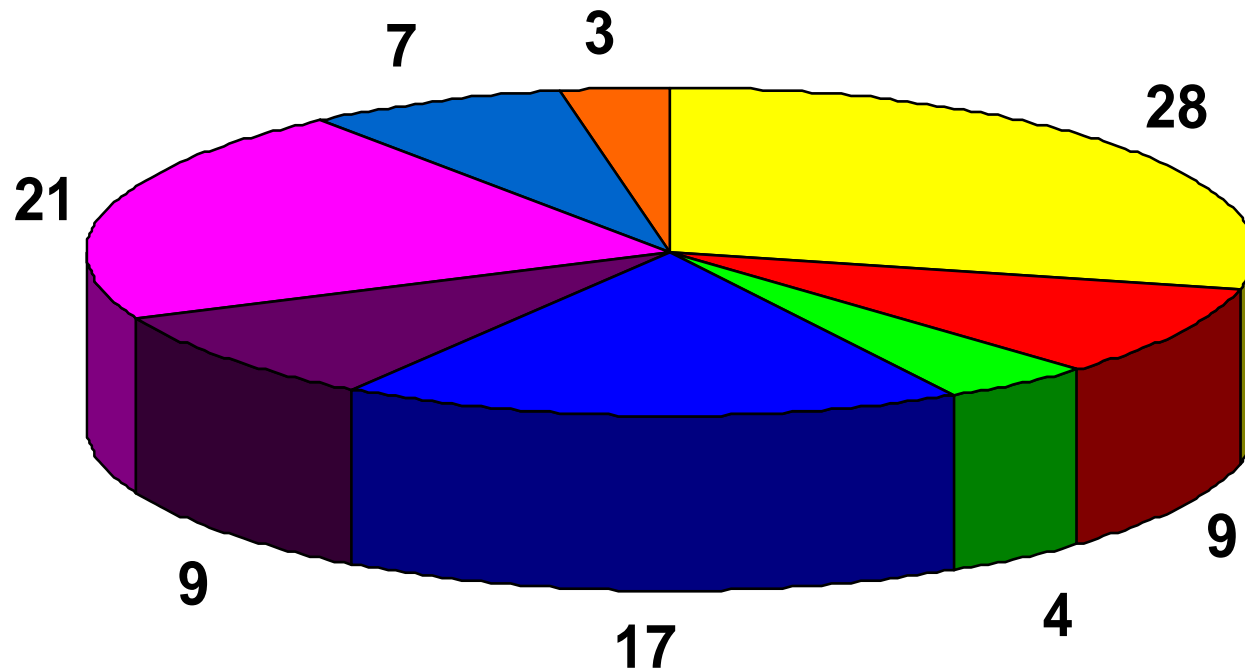
Methods: Predictors of MDS

- **Statistical analysis for important predictors of confirming MDS**
- **A score function (Sf) was derived from significant predictive factors to estimate the probability for finding MDS**



Results

322/2267 (14%) bone marrows met inclusion criteria

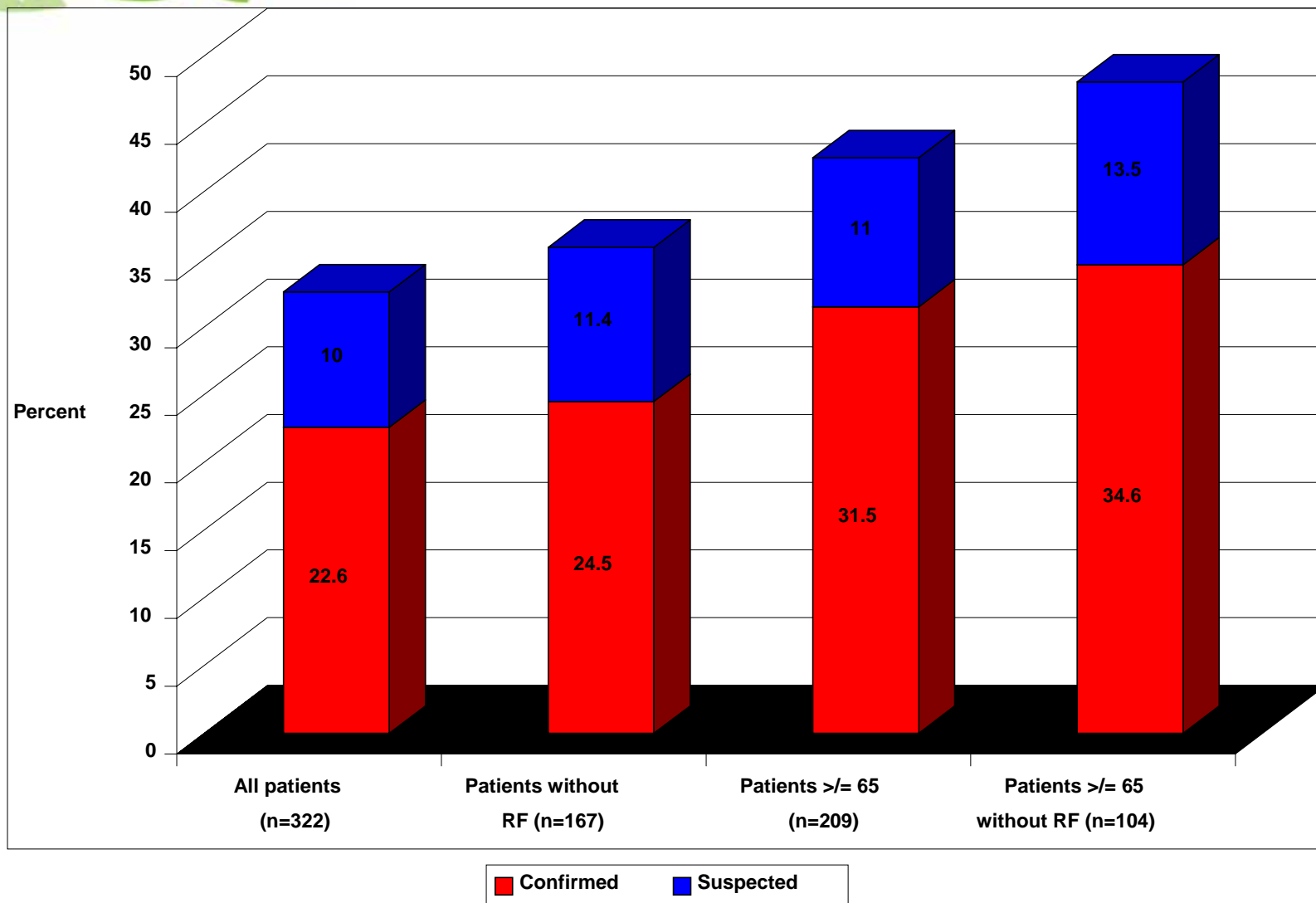


■ A ■ T ■ L ■ A+T ■ A+N ■ A+T+N ■ T+N ■ Other

BM Diagnosis

All patients

# confirmed MDS (%)	73 (23%)
# suspected MDS (%)	32 (10%)
# normal (%)	54 (17%)
# not diagnostic (%)	78 (24%)
# other	85 (26%)





Let's do the math.....

- 2006 Canadian census data
- 13.7% aged ≥ 65 = 4,330,996
- If 10.2% anemic and 35% are unexplained and 32% are MDS by BM then speculated prevalence: **49,476 cases in Canada**
- If 2.2% anemic: **10,671 cases in Canada**

Or

2/1000 over age 65



Limitations

- Looking back study: not all information was available
- Patient populations different from that in the NHANES US study
- The bone marrows were not reviewed by outside pathologists



Conclusions

- 22.6% of patients with undiagnosed cytopenia(s) had confirmed MDS and 10% had suspected MDS by bone marrow analysis
- In patients ≥ 65 the frequency of confirmed MDS increased to 31.5% and suspected 11%
- age ≥ 65 , increased red cell size, red cell distribution width, LDH at the time of investigative bone marrow increases the likelihood of diagnosing MDS.
- Given the prevalence of elderly anemia in North America, MDS prevalence is likely higher than initially speculated



Summary

- The incidence of MDS increases significantly with age and is more common in men
- The prevalence of MDS may be higher than we thought....
- Efforts to increase diagnosis should be made
- The health care burden of MDS will increase significantly in years to come



Acknowledgements

- **ASH summer studentship award**
- **Karen Jang**
- **Department of Hematopathology**
- **Crashley Estate Endowment to MDS Program**
- **Richard Wells**

Thank You!