

# Monoclonal Gammopathy of Undetermined Significance (MGUS)

**The Plummer Society**

**October 30, 2009**

**Scottsdale, AZ**

**Robert A. Kyle, MD**



**Scottsdale, Arizona**



**Rochester, Minnesota**



**Jacksonville, Florida**

# DISCLOSURE

**Relevant Financial Relationship:**

**None**

**Off Label Usage:**

**None**

# **MGUS: Olmsted County, Minnesota Inclusion Criteria**

- **Serum M-spike <3.0 g/dL**
- **Bone marrow plasma cells <10% (if done)**
- **No evidence of other B-cell disorders**
- **No end-organ damage**

# **MGUS: Olmsted County, Minnesota Prevalence Study**

- **Olmsted County residents  $\geq 50$  years: 28,038**
- **Serum samples obtained from population: 77%**

**Kyle et al: New Engl J med 354:1362, 2006**

# MGUS: Olmsted County, Minnesota

<b>Age</b>	<b>No.</b>	<b>M-protein</b>	
		<b>No.</b>	<b>%</b>
<b>50 – 59</b>	<b>8,373</b>	<b>141</b>	<b>1.7</b>
<b>60 – 69</b>	<b>6,019</b>	<b>178</b>	<b>3.0</b>
<b>70 – 79</b>	<b>4,508</b>	<b>205</b>	<b>4.6</b>
<b>≥80</b>	<b>2,563</b>	<b>170</b>	<b>6.6</b>
<b>Total</b>	<b>21,463</b>	<b>694</b>	<b>3.2</b>
<b>≥ 70</b>	<b>7,071</b>	<b>375</b>	<b>5.3</b>

# MGUS Precedes MM

PCLO Study  
N = 77,469

	N
Developed MM	71

Landgren et al., Blood 113:5412, 2009

# MGUS Present Before DX MM

Years	%
2	100
3	98
5	95
7	93
8+	82

Landgren et al., Blood 113:5412, 2009

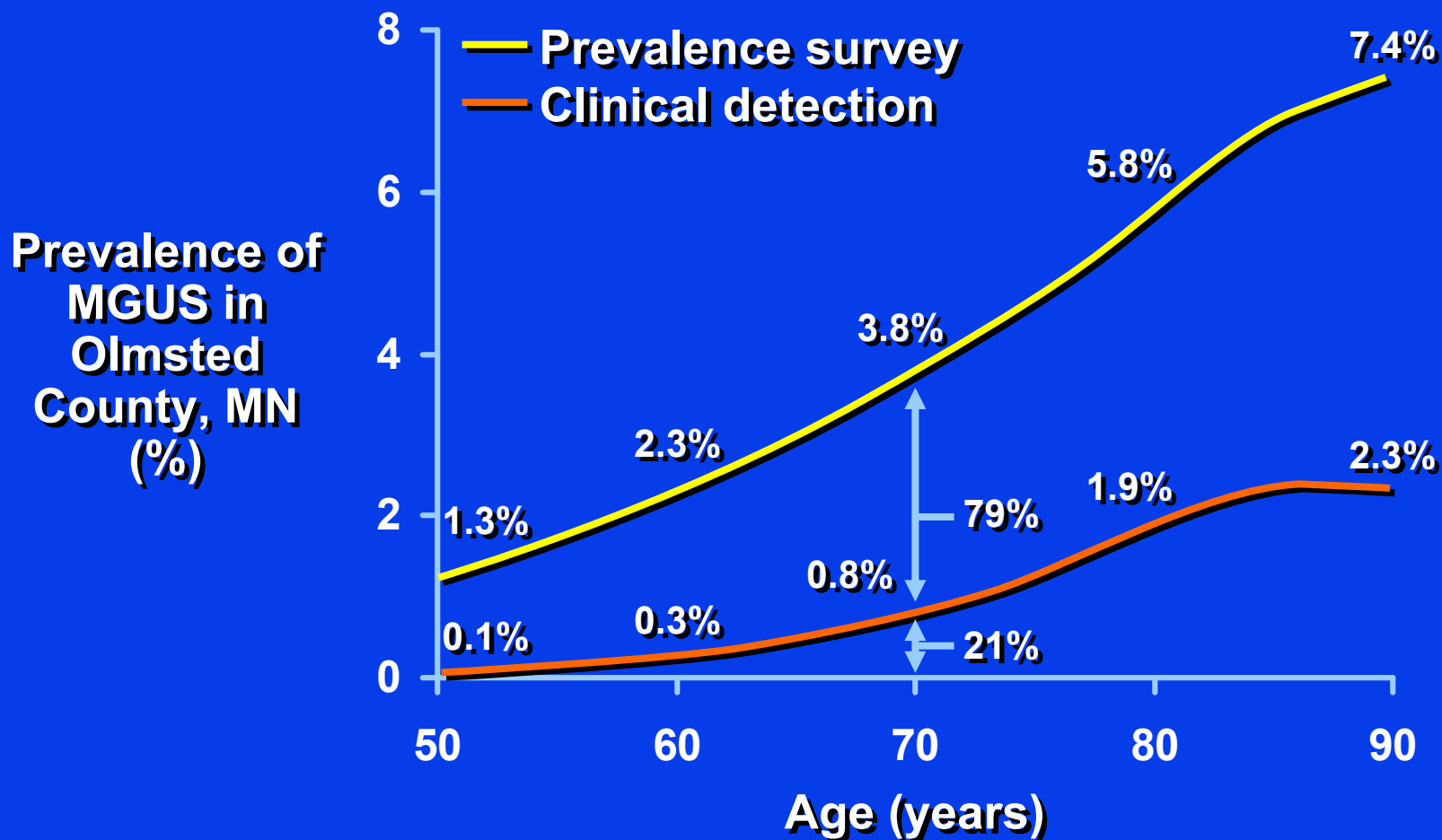
# MGUS

**Virtually all patients with multiple myeloma have a previously recognized M-protein (MGUS).**

# MGUS

**How many patients with  
MGUS are recognized  
during clinical practice at  
Mayo Clinic?**

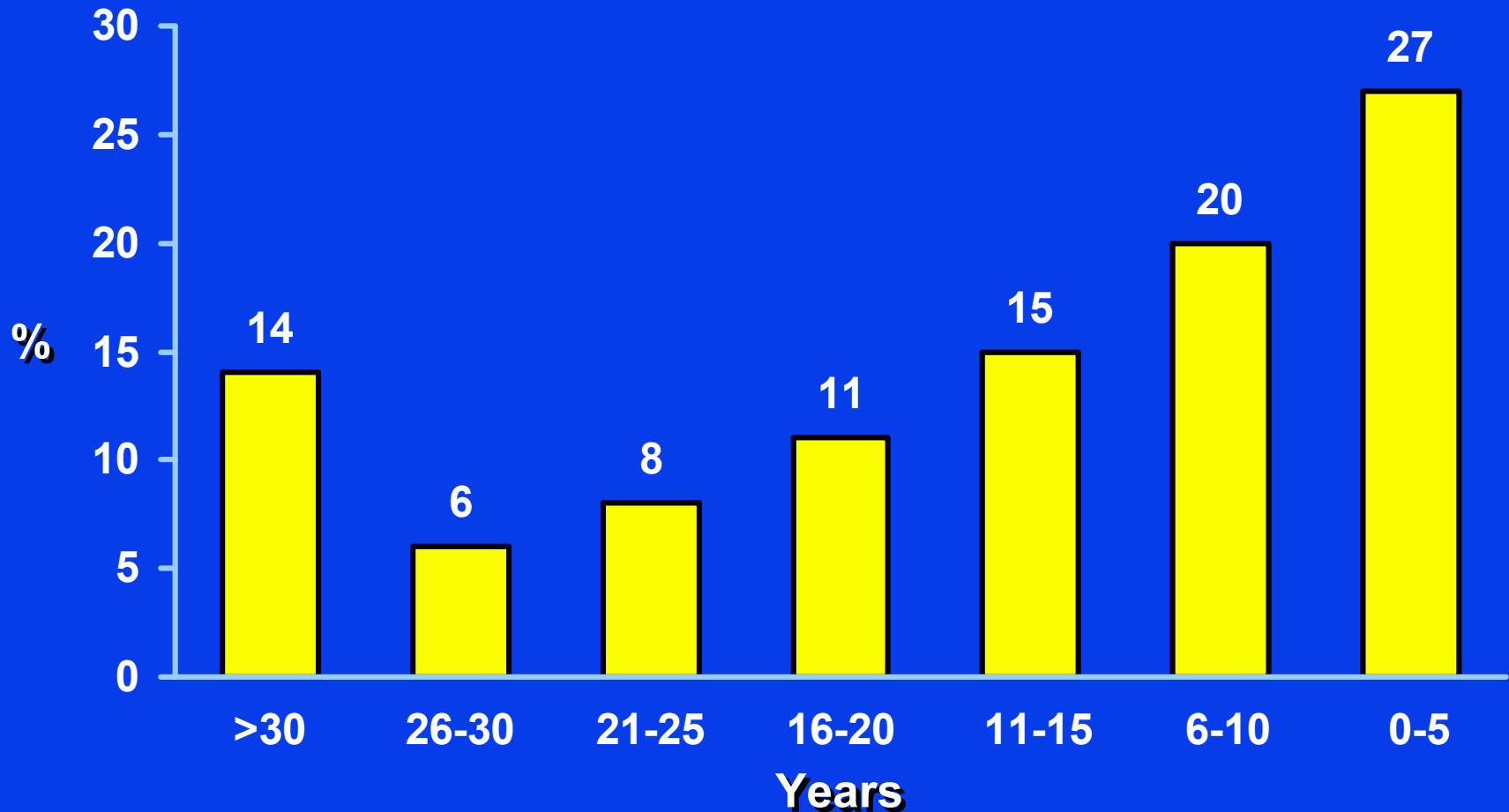
# MGUS: Prevalence in Olmsted County, MN vs Clinical Detection



# MGUS

**How long has MGUS  
been present when it  
is recognized?**

# Duration of MGUS for A Patient At Age 70



# Monoclonal Gammopathy of Undetermined Significance (MGUS): Conclusions

- **Only 22% with known MGUS have been recognized clinically**
- **28% recognized as MGUS at age 70 have had it >20 years**
- **Median duration of MGUS prior to its recognition = 11 years**

# **Monoclonal Gammopathy of Undetermined Significance Natural History in 241 Cases**

**241 patients with a protein in the serum  
but initially no evidence of multiple  
myeloma, macroglobulinemia,  
amyloidosis, or lymphoma 1956-1970 were  
followed up.**

**Kyle RA, Am J Med 64:814, 1978**

# MGUS

## Status at Follow-Up 1-39 Years ( 241 Cases)

Group	Description	Follow-up Person-years 3,579 Median	
		No.	%
1	No substantial increase of M-protein (benign)	14	6
2	Increase M-protein ( $\geq 3$ g/dL)	25	10
3	Died of unrelated causes	138	57
4	Development of myeloma, macroglobulinemia, amyloidosis, etc	64	27
<b>Total</b>		<b>241</b>	<b>100</b>

Kyle et al., Mayo Clinic Proceed 79:859, 2004

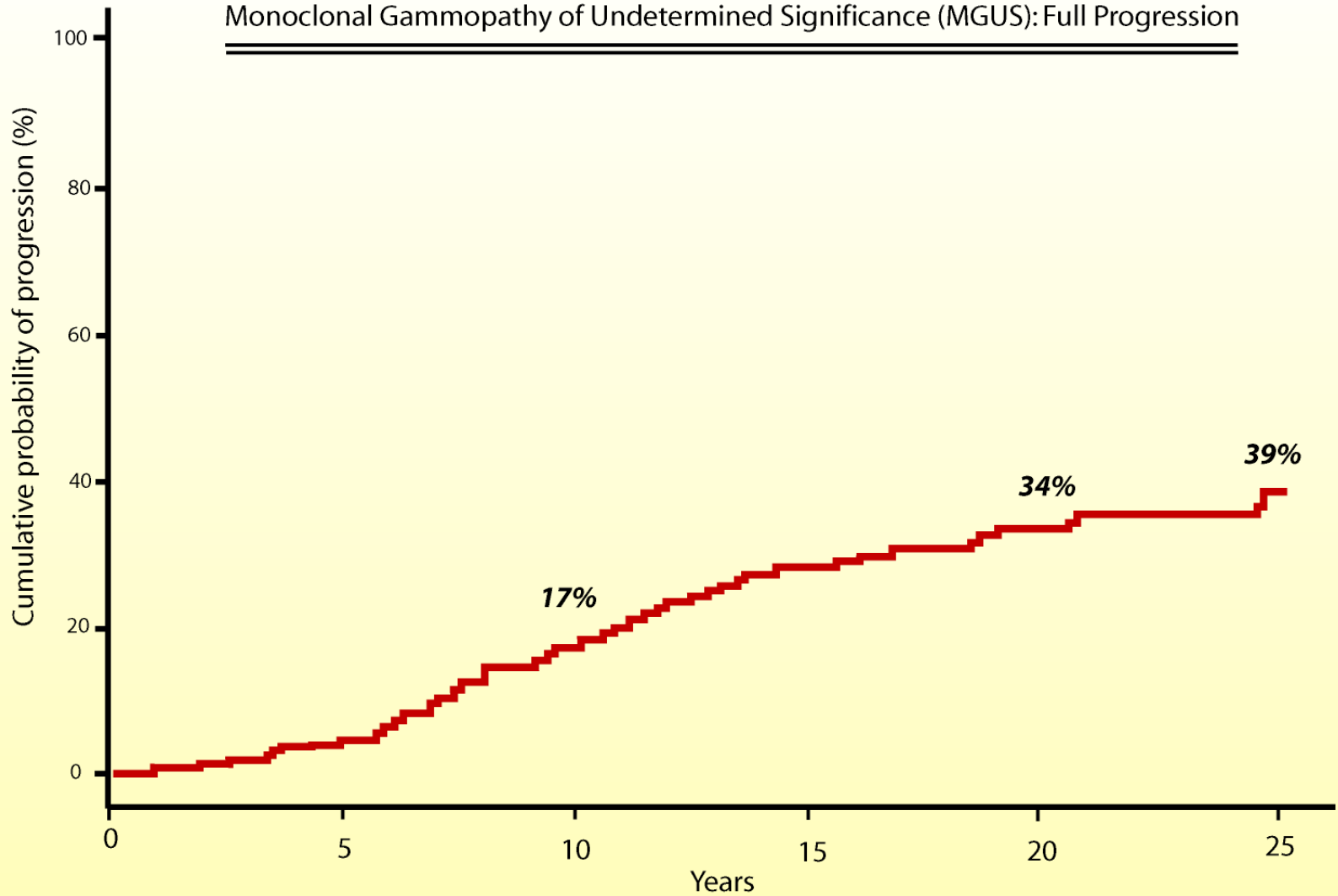
# MGUS

## Development of Myeloma or Related Disease in 64 Patients with MGUS

	No.	%	Interval to disease (yr)	
			Median	Range
Multiple myeloma	44*	69	10.6	1-32
Macroglobulinemia	7	11	10.3	4-16
Amyloidosis	8	12	9.0	6-19
Lymphoproliferative disease	5	8	8.0	4-19
<b>Total</b>	<b>64</b>	<b>100</b>	<b>10.4</b>	<b>1-32</b>

\*Dx of myeloma made after 20-yr F-U in 10 pt

Monoclonal Gammopathy of Undetermined Significance (MGUS): Full Progression



Mayo Clinic Proceedings 2004; 79:859, Kyle et al.

# **MGUS**

## **SE Minnesota**

### **Jan 1, 1960-Dec 31, 1994**

**N = 1,384**

<b>Male (%)</b>	<b>54</b>
<b>Age (med years)</b>	<b>72</b>
<b>&lt;40 years (%)</b>	<b>1.7</b>
<b>M-spike (g/dL-med)</b>	<b>1.2</b>

Kyle, et al., New Engl J Med, 346:564, 2002

# MGUS SE MINNESOTA

## Relative Risk of Progression

	Obs	Exp*	RR
Multiple Myeloma	75	3	25
Lymphoma	19	7.8	2.4
Amyloidosis	10	1.2	8.4
Macroglobulinemia	7	0.2	46
CLL	3	3.5	0.9
Plasmacytoma	1	0.1	8.5
Total	115	15.8	7.3

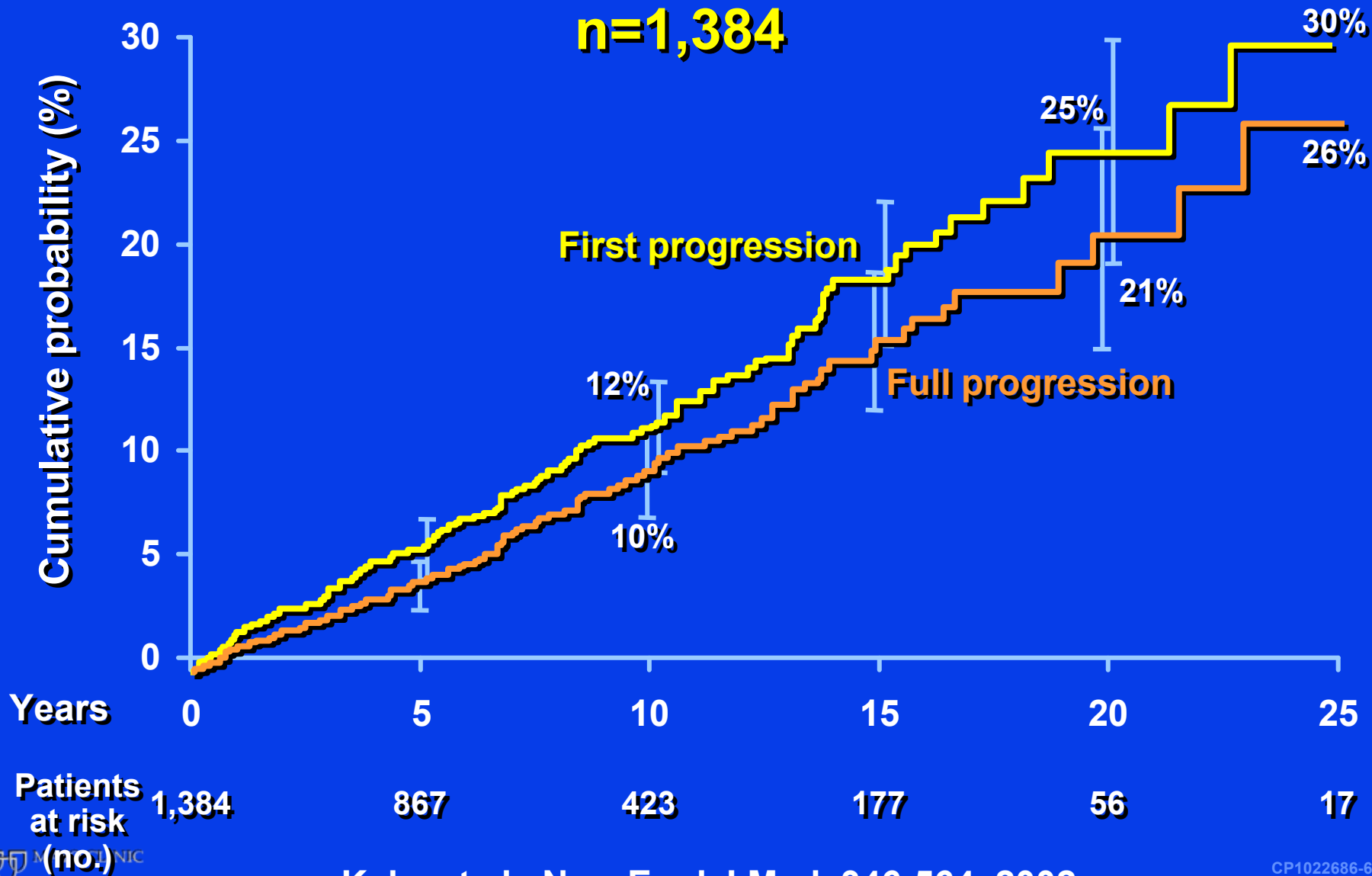
\* Iowa SEER Registry

Kyle, et al., New Engl J Med, 346:564, 2002

# MGUS SE Minnesota

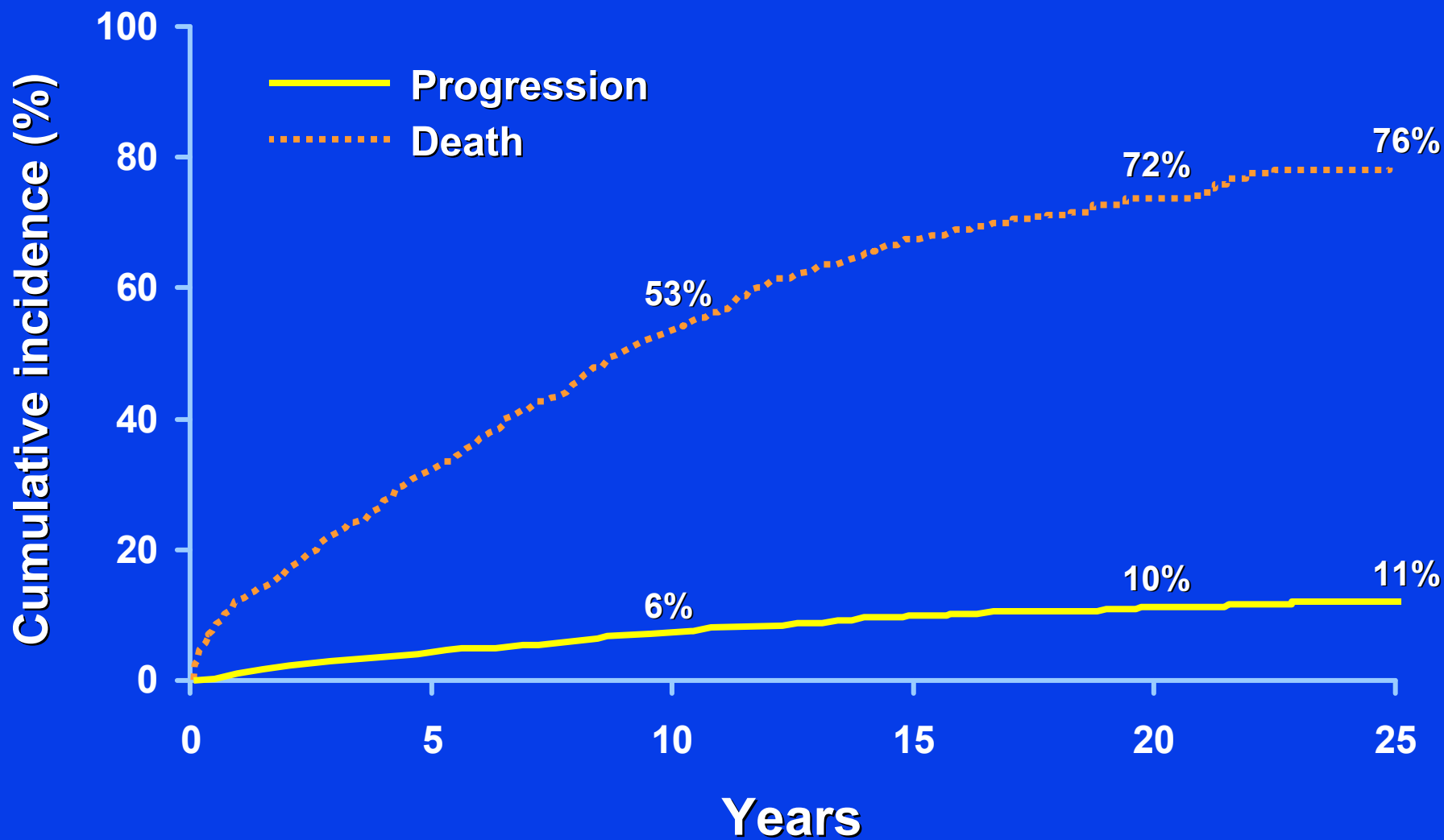
1960-1994

n=1,384



Kyle, et al., New Engl J Med, 346:564, 2002

# Full Progression or Death



# MGUS SE Minnesota Summary

- **MGUS patients more likely to die of unrelated disease than to progress**
- **Myeloma accounts for 65% of progression**
- **Risk of progression is 1%/year**
- **Risk of progression associated with size and type of M-protein and FLC**

