

Use of G-CSF in elderly patients

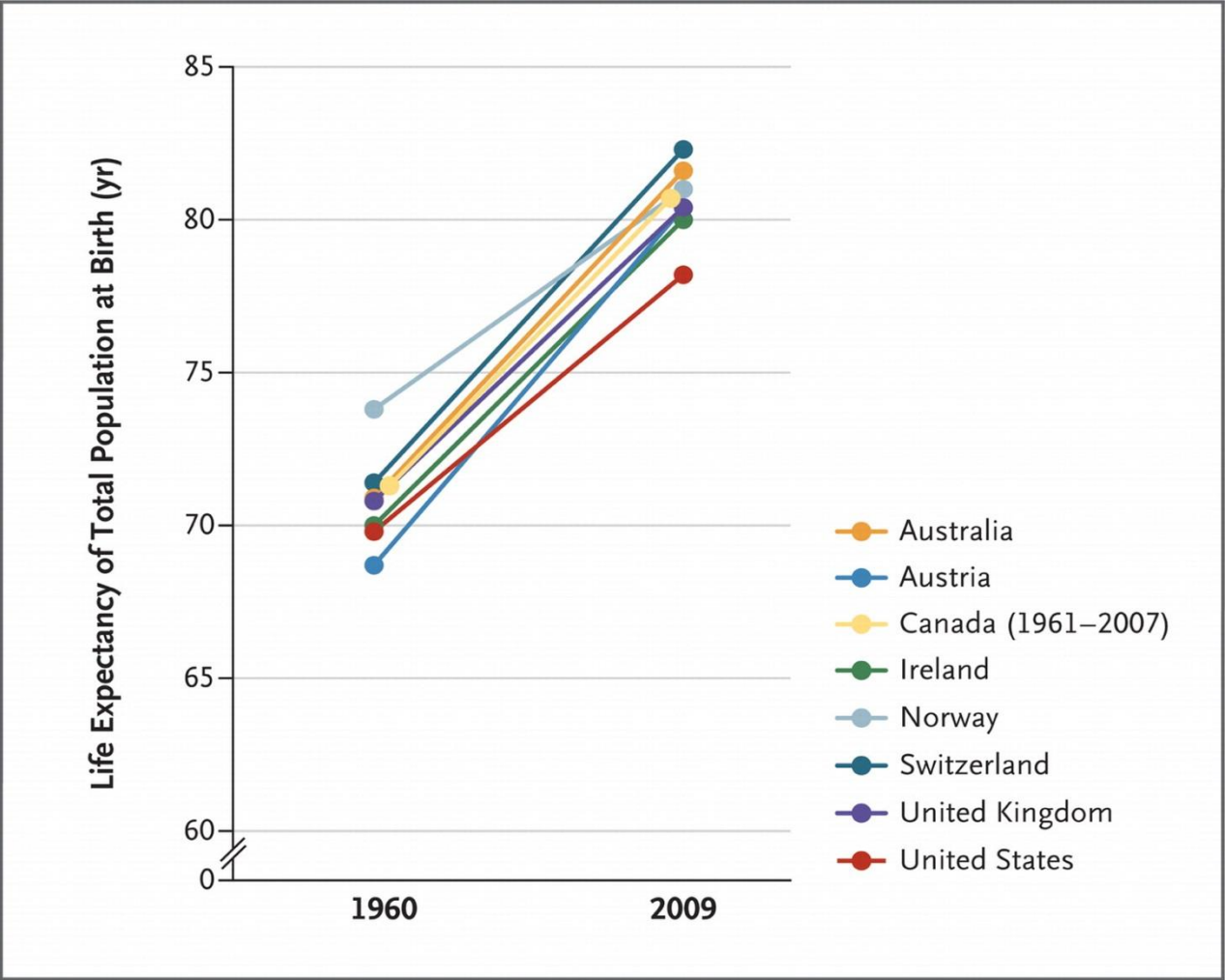
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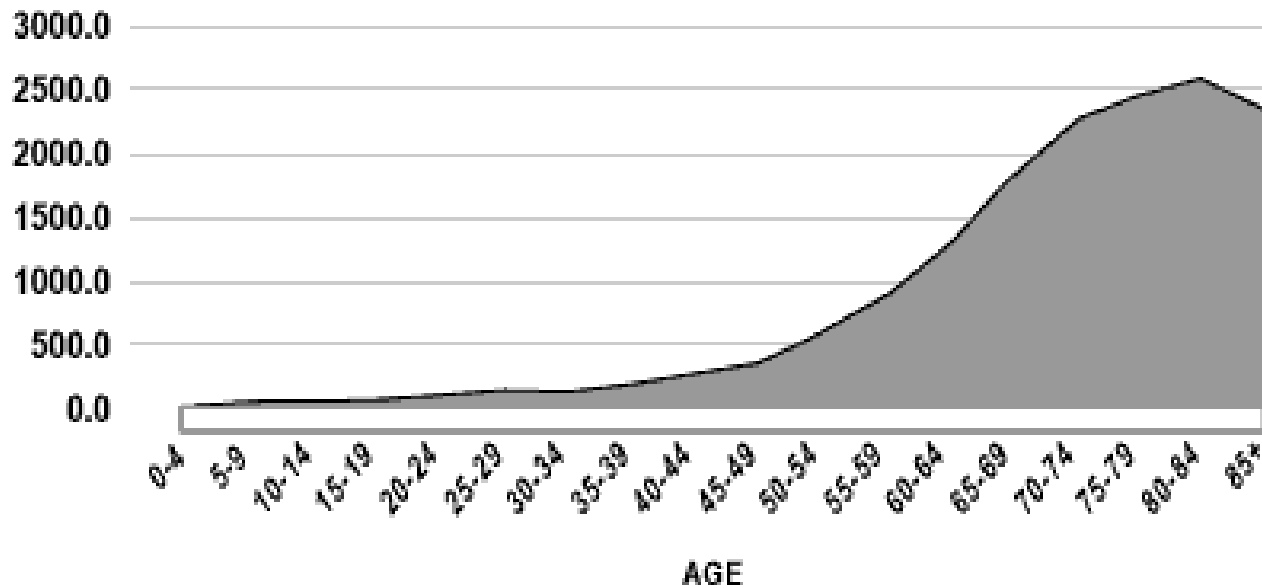
Life Expectancy at Birth in Selected OECD Countries, 1960–2009.



Aging and cancer

Figure 1. Cancer Incidence by Age Group, All Sites Combined, Both Sexes

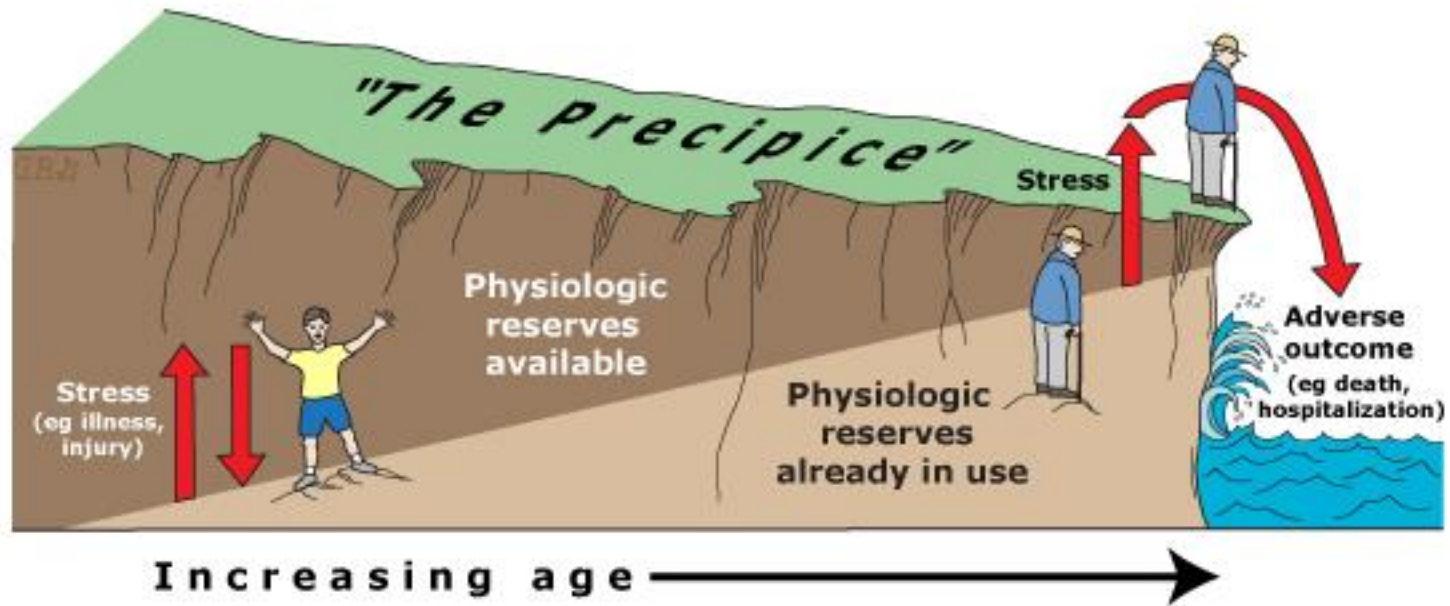
Rate per 100,000 Population



Source: NCI SEER Program Data, 1994–98

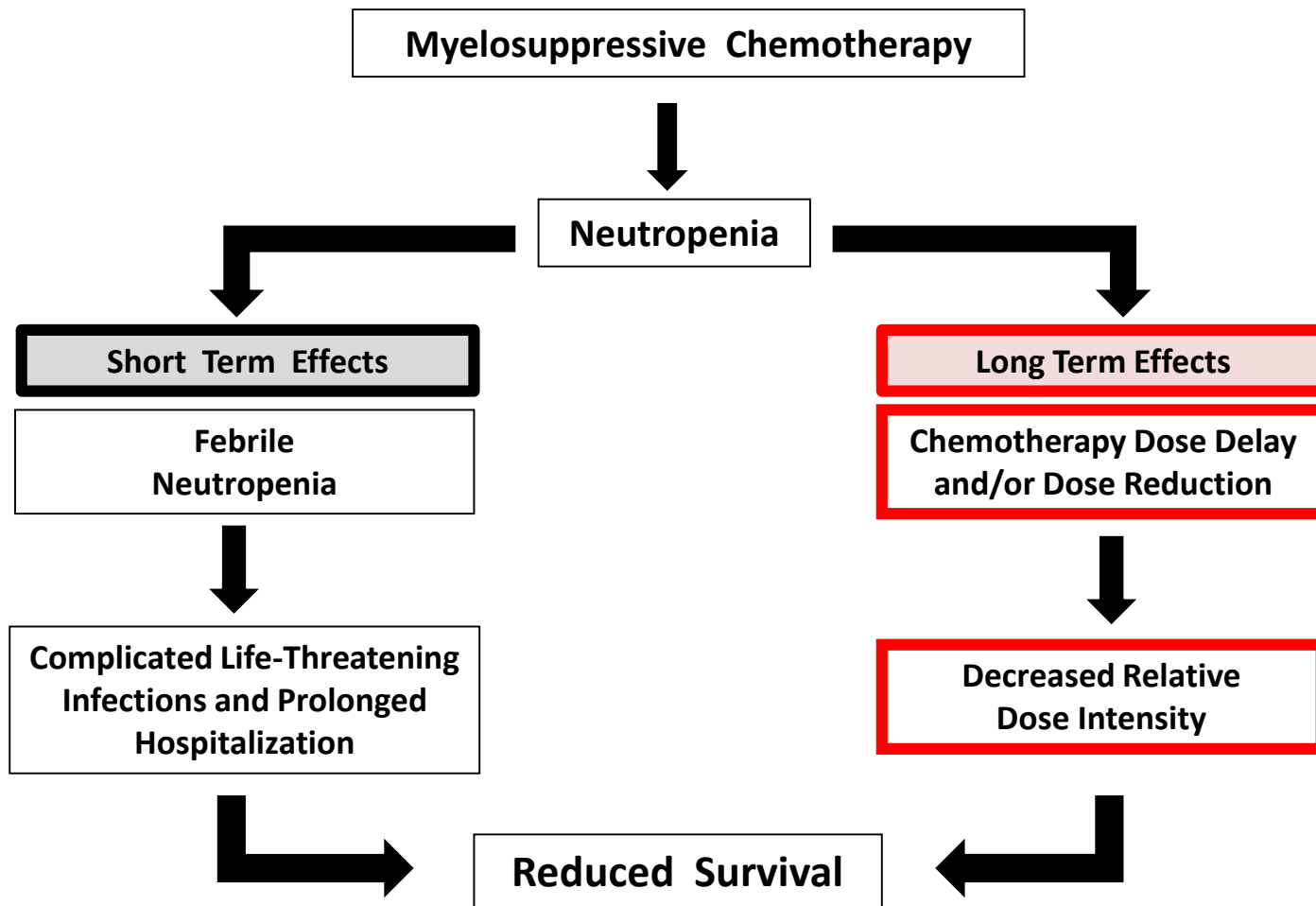
Homeostenosis leads to the increased vulnerability to disease that occurs with aging.

Homeostenosis



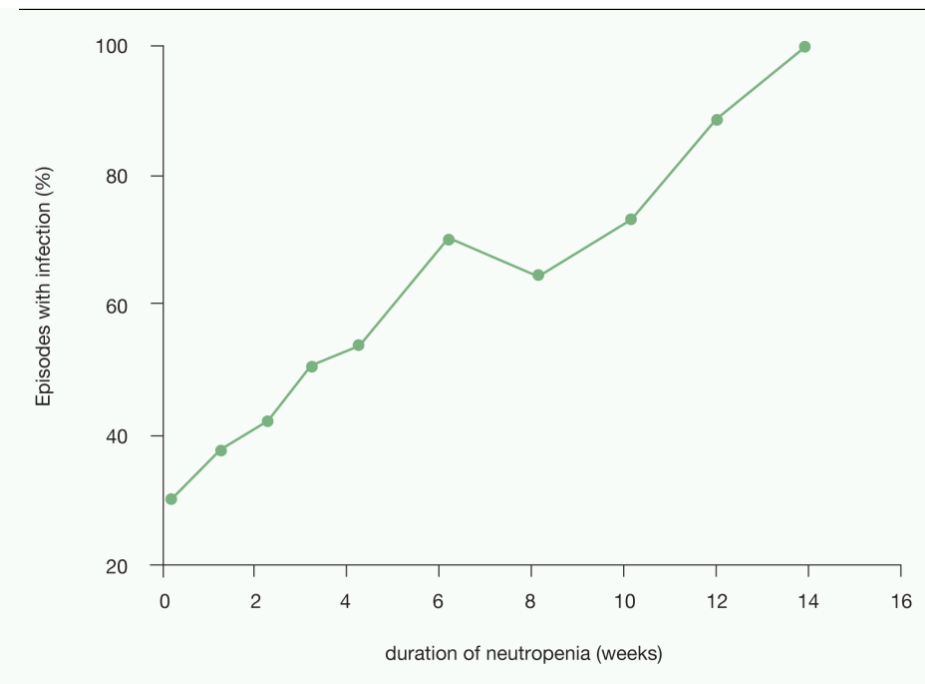
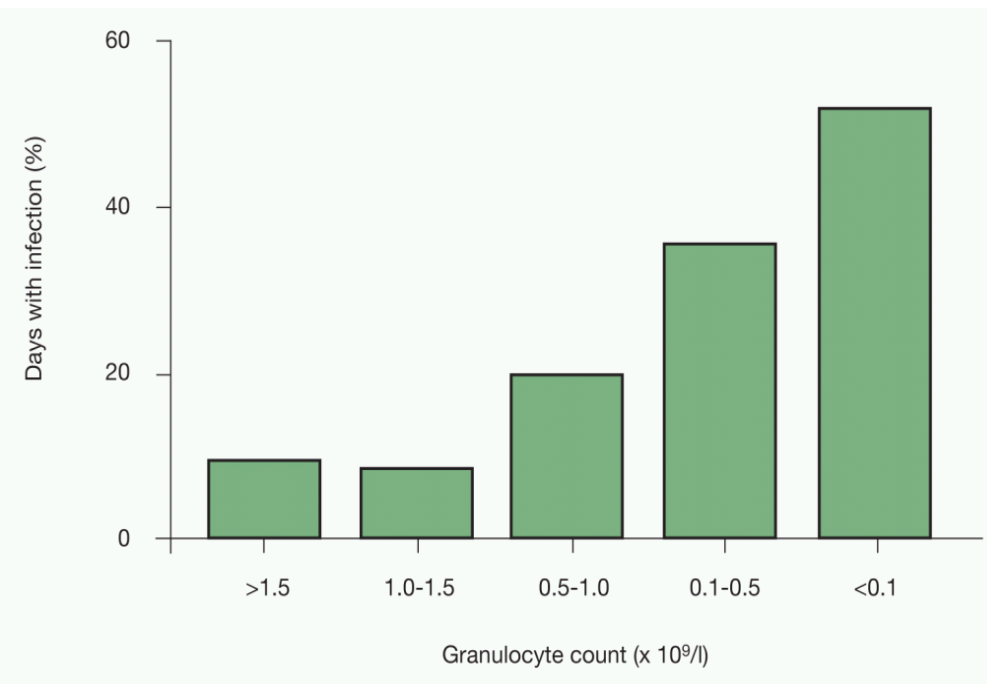
Based on information from: Taffet GE. Physiology of aging. In: Cassel CK, Leipzig RM, Cohen HJ, et al [eds]. *Geriatric Medicine: An Evidence-Based Approach*, 4th ed. New York, Springer, 2003.

Short and Long-Term Consequences of CIN / FN Daily Clinical Practice



Bonadonna G et al. N Engl J Med. 1995 ; Leonard RCF et al. Br J Cancer 2003;
Kuderer NM et al. J Clin Oncol. 2004 ; Bosly A et al. Ann Hematol. 2008;
Lyman GH et al. Cancer 2010; Aapro M et al. Eur J Cancer 2011.

THE RISK OF INFECTION INCREASES WITH THE SEVERITY AND DURATION OF NEUTROPENIA



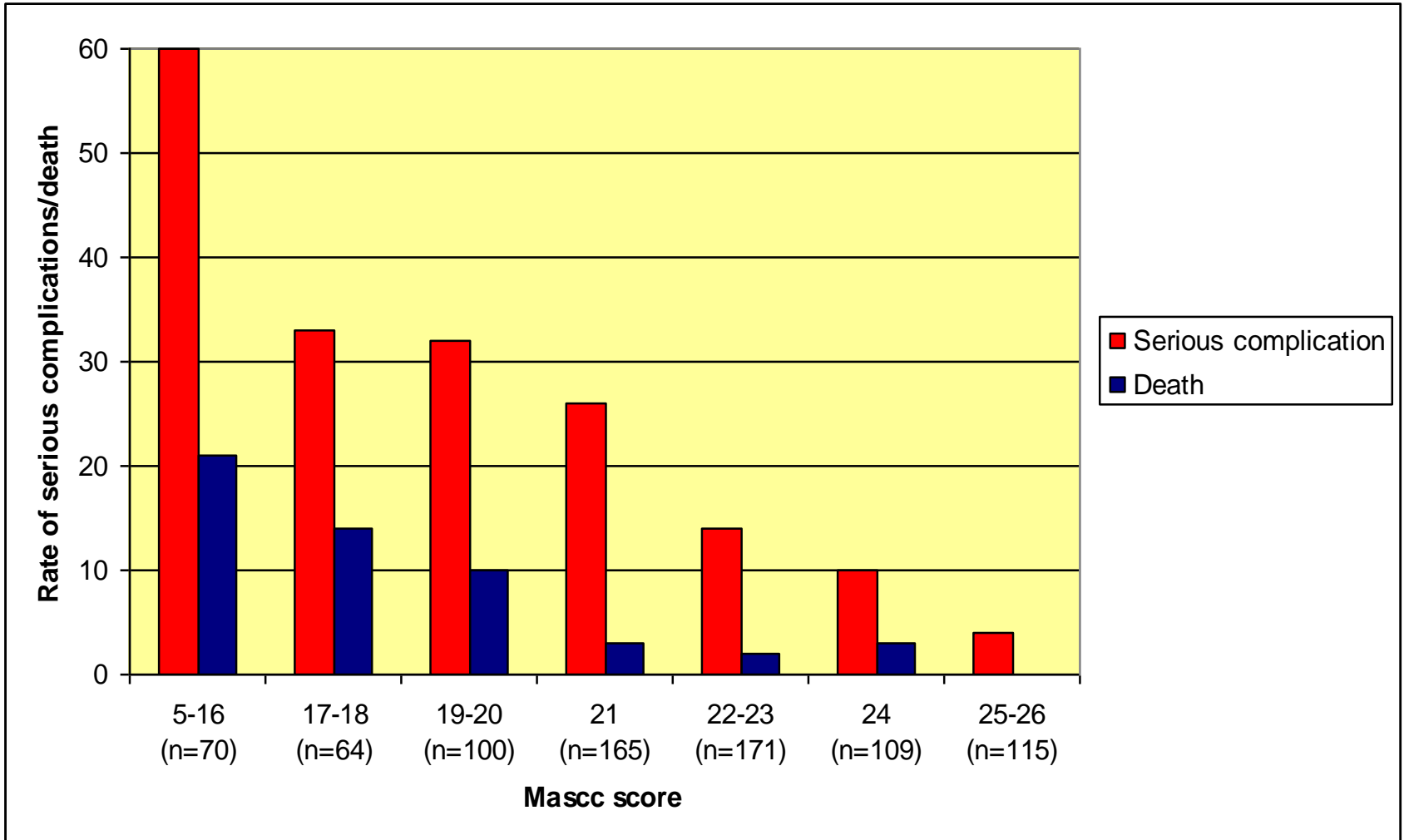
G.P. Bodey, Ann Int Med, 1966

Multinational Association of Supportive Cancer Care scoring system

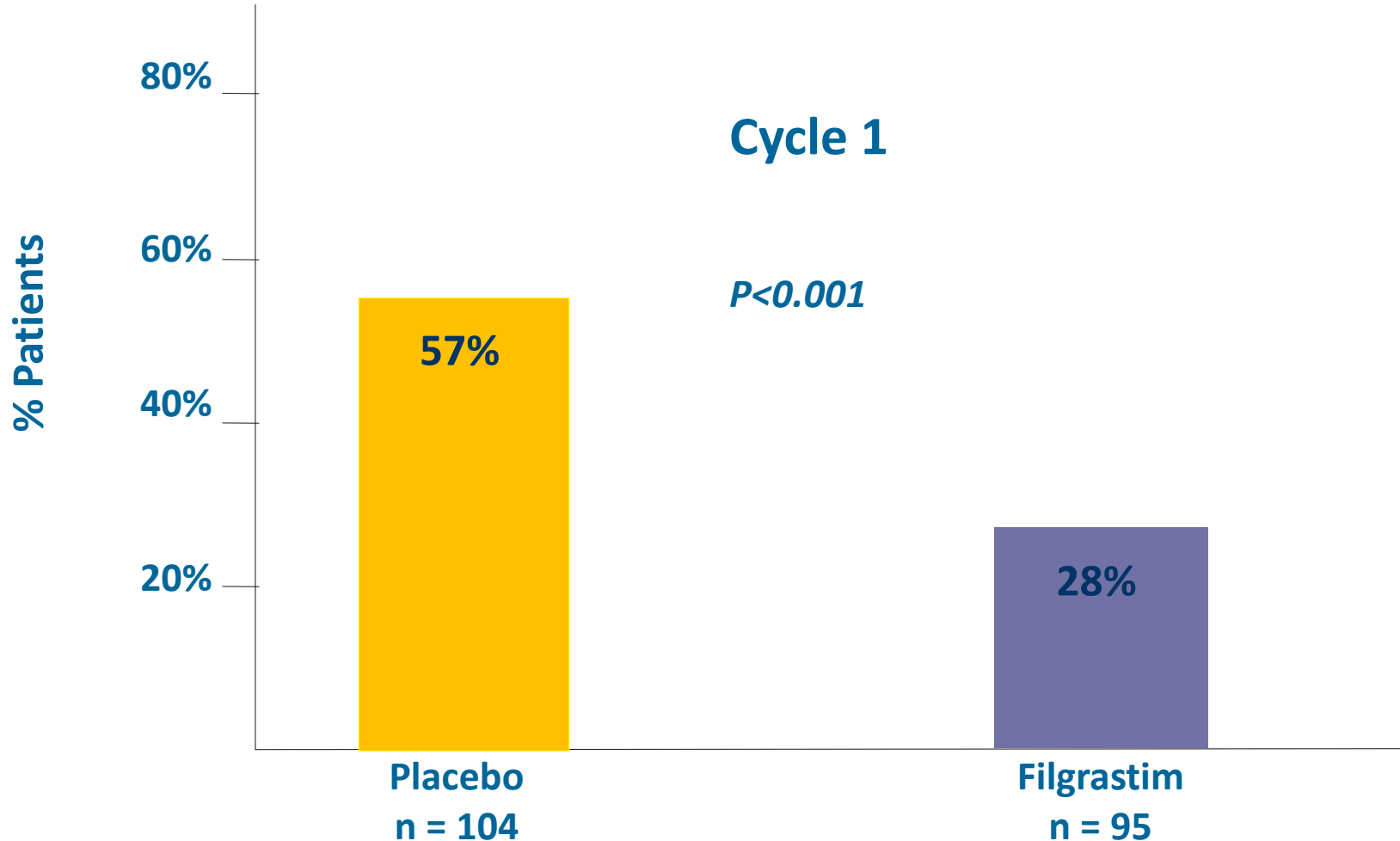
Characteristic	Weight
Burden of illness: no or mild symptoms	5
No hypotension	5
No chronic obstructive pulmonary disease	4
Solid tumor or no previous fungal infection	4
No dehydration	3
Burden of illness: moderate symptoms	3
Outpatient status	3
<u>Age <60 years</u>	2

A MASCC score index ≥ 21 predicts
a low (5-10%) risk of complications and death (<2%)

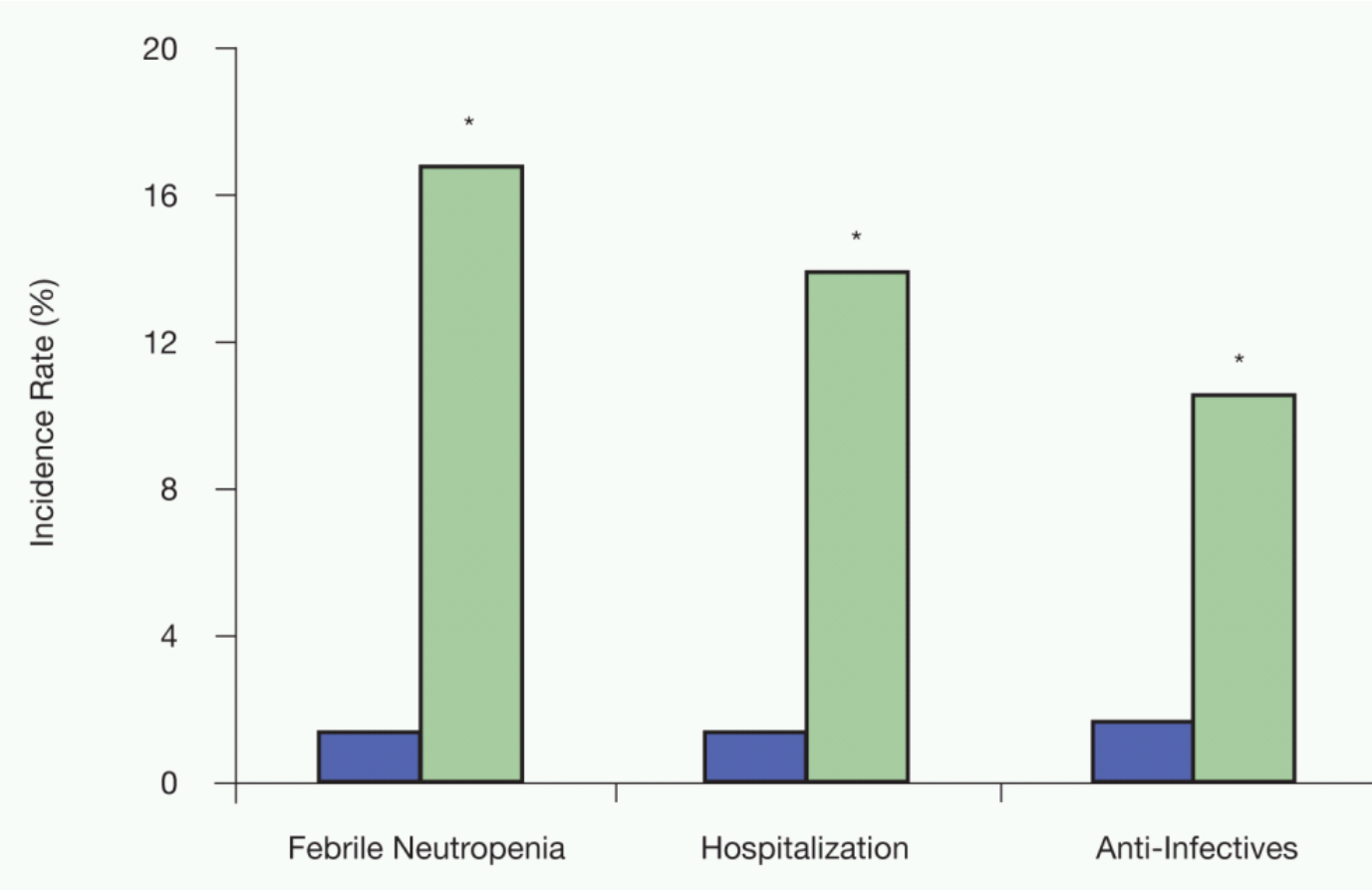
Predicting high risk ?



FILGRASTIM REDUCES INCIDENCE OF FEBRILE NEUTROPENIA



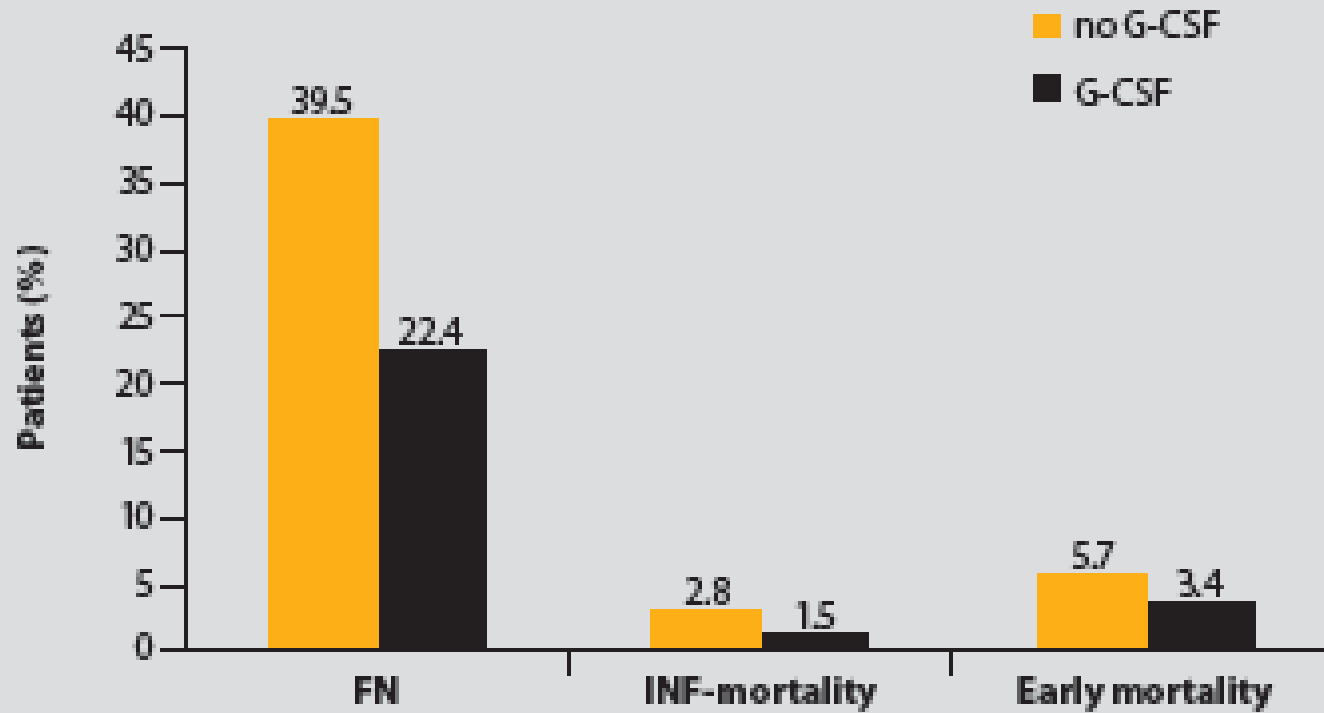
PEGFILGRASTIM VS PLACEBO IN BREAST CANCER PATIENTS: IMPACT ON NEUTROPENIA-RELATED EVENTS



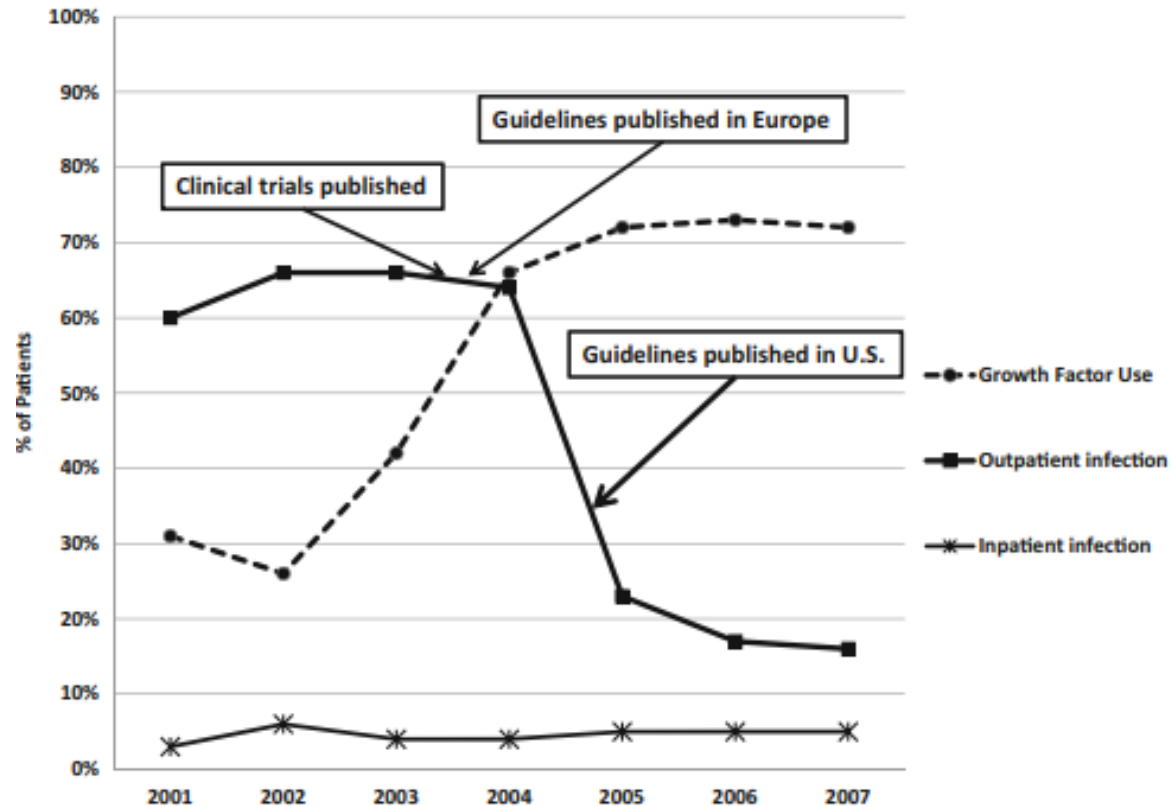
Pegfilgrastim (n=463) reduces the incidence of FN compared to a placebo (n=465) and the need for hospitalization and intravenous anti-infectives as a result of FN
*** P<001**

Vogel et al., JCO, 2005

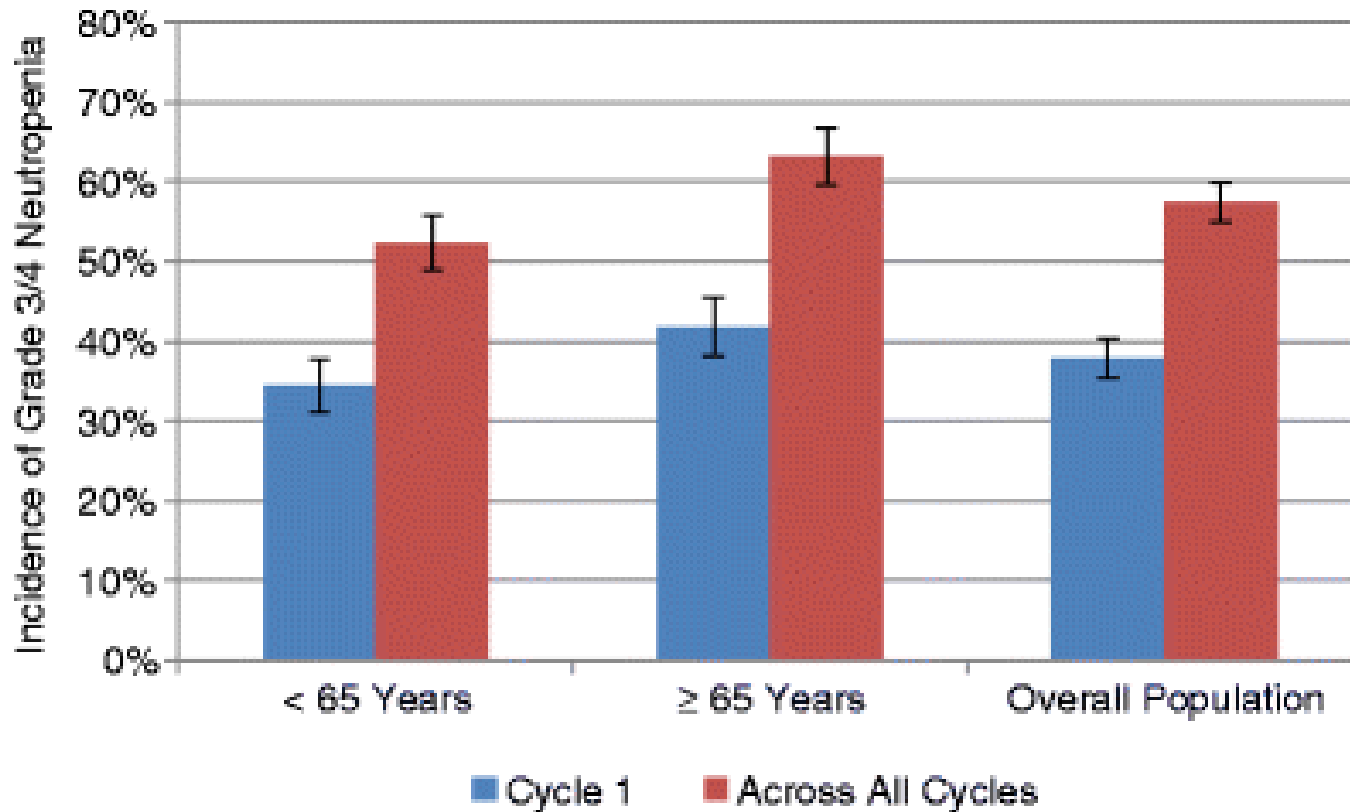
Effect on febrile neutropenia and mortality



Relationship between inpatient or outpatient infections and the use of G-CSFs

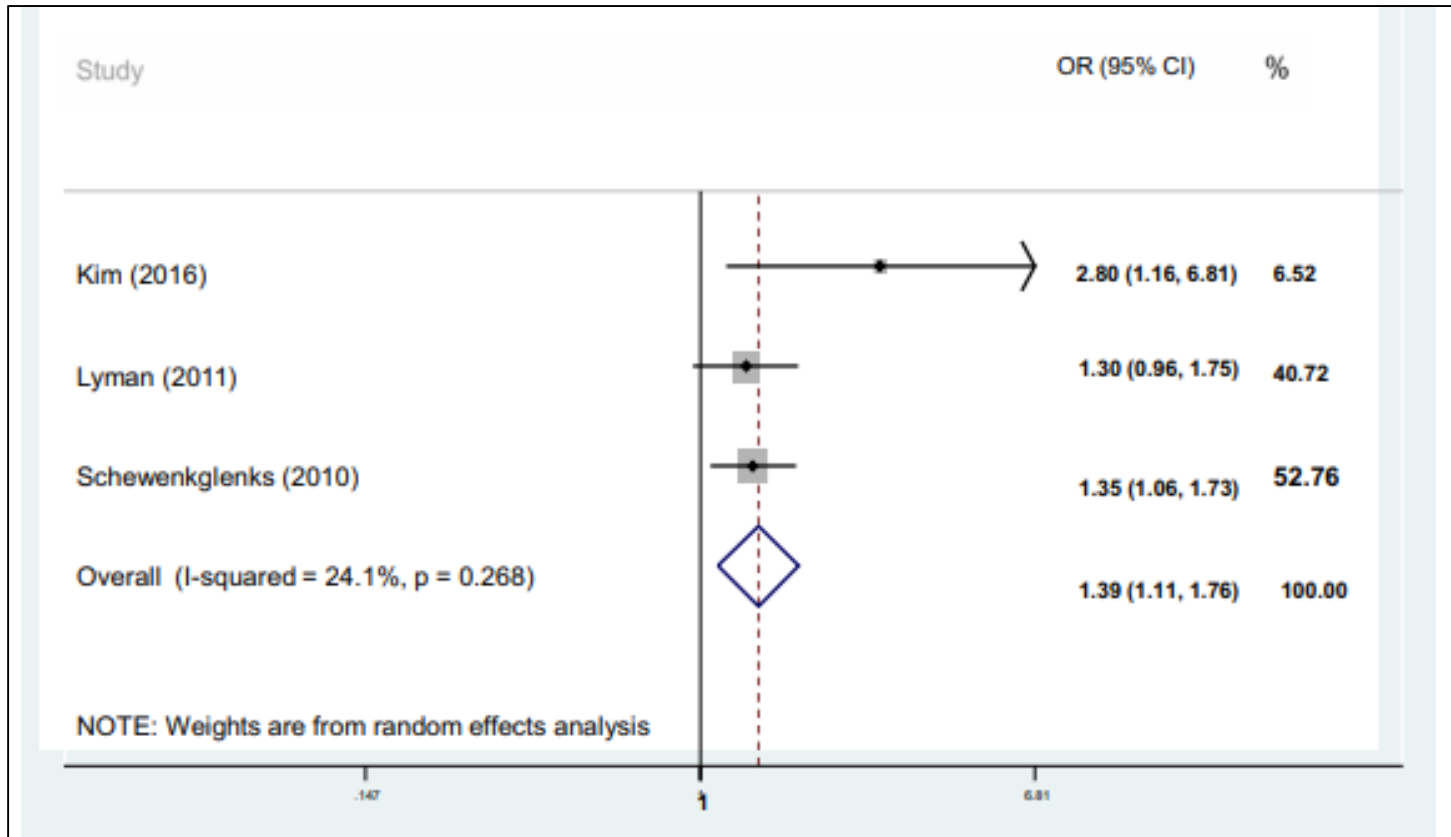


OLDER NON HK-LYMPHOMA PATIENTS RECEIVING CHOP

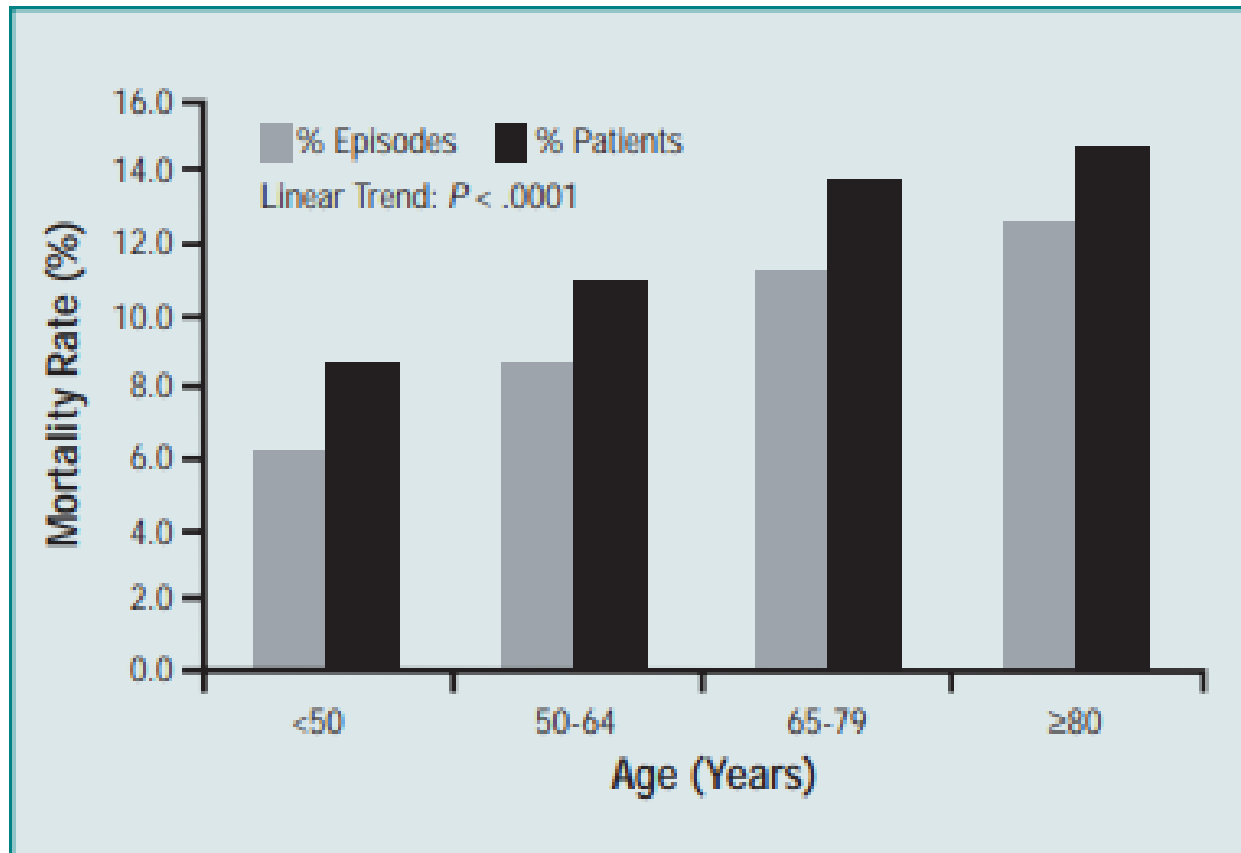


Grade 3/4 neutropenia in cycle 1 and across all cycles. Incidences and 95% CIs are shown.

SUBGROUP ANALYSIS SHOWING POOLED ODDS OF NEUTROPENICS EVENTS >65 YEARS



Risk of mortality across age groups among patients admitted for FN



INFLUENCE OF **AGE** ON NEUTROPENIA-RELATED EVENTS

Incidence: 6 cycles	≥ 65 years (N=172)	< 65 years (N=110)
FN	17%	12%
Hospitalization due to FN	13%	6%
Use of anti-infectives	66%	48%
Dose delays > 3 days	26%	25%
Dose reduction > 10%	52%	29%
RDI ≥ 90%	78%	89%

PROSPECTIVE ANALYSIS EVALUATING RATES OF DOSE DELAY/REDUCTIONS, RDI<85% BY AGE GROUPS AND DISEASE STAGES IN ELDERLY POPULATION

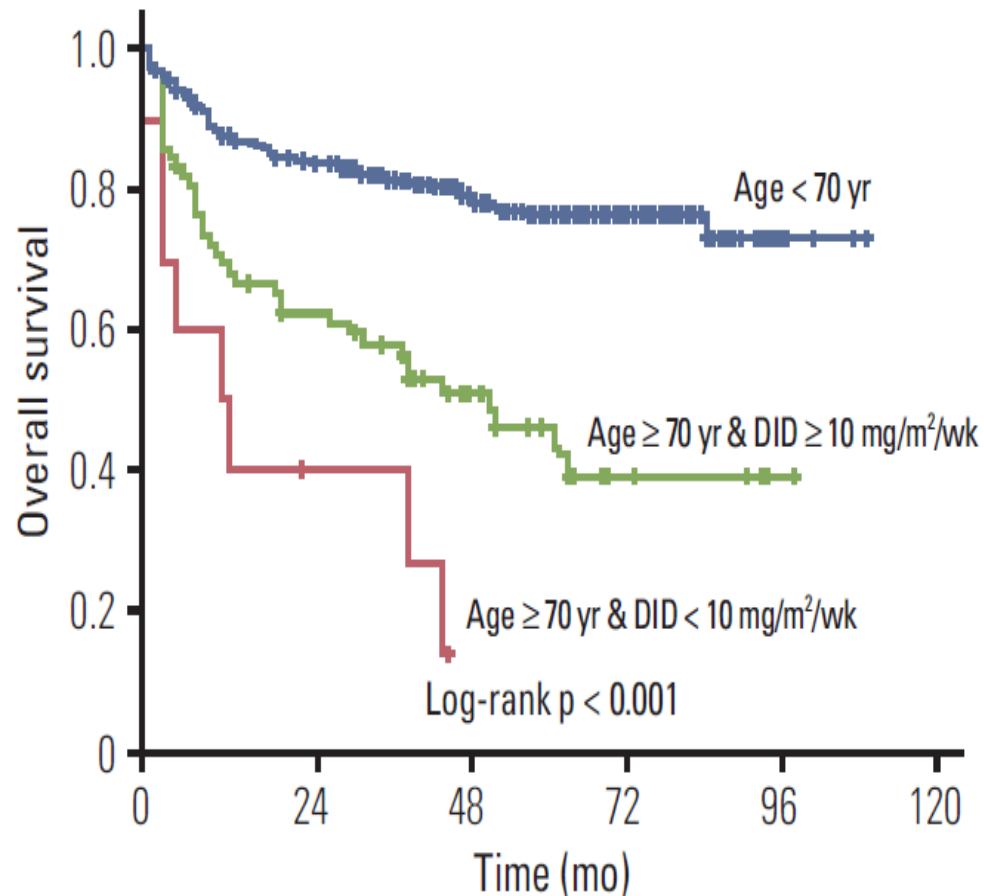
	Age 70-74 (n=305)	Age 75-79 (n=216)	Age ≥ 80 (n=136)
Dose Delay ≥ 15%	30%	29%	39%
Dose Reduction ≥ 15%	42%	43%	51%
RDI ≤ 85%	51%	46%	60%

RDI: relative dose intensity

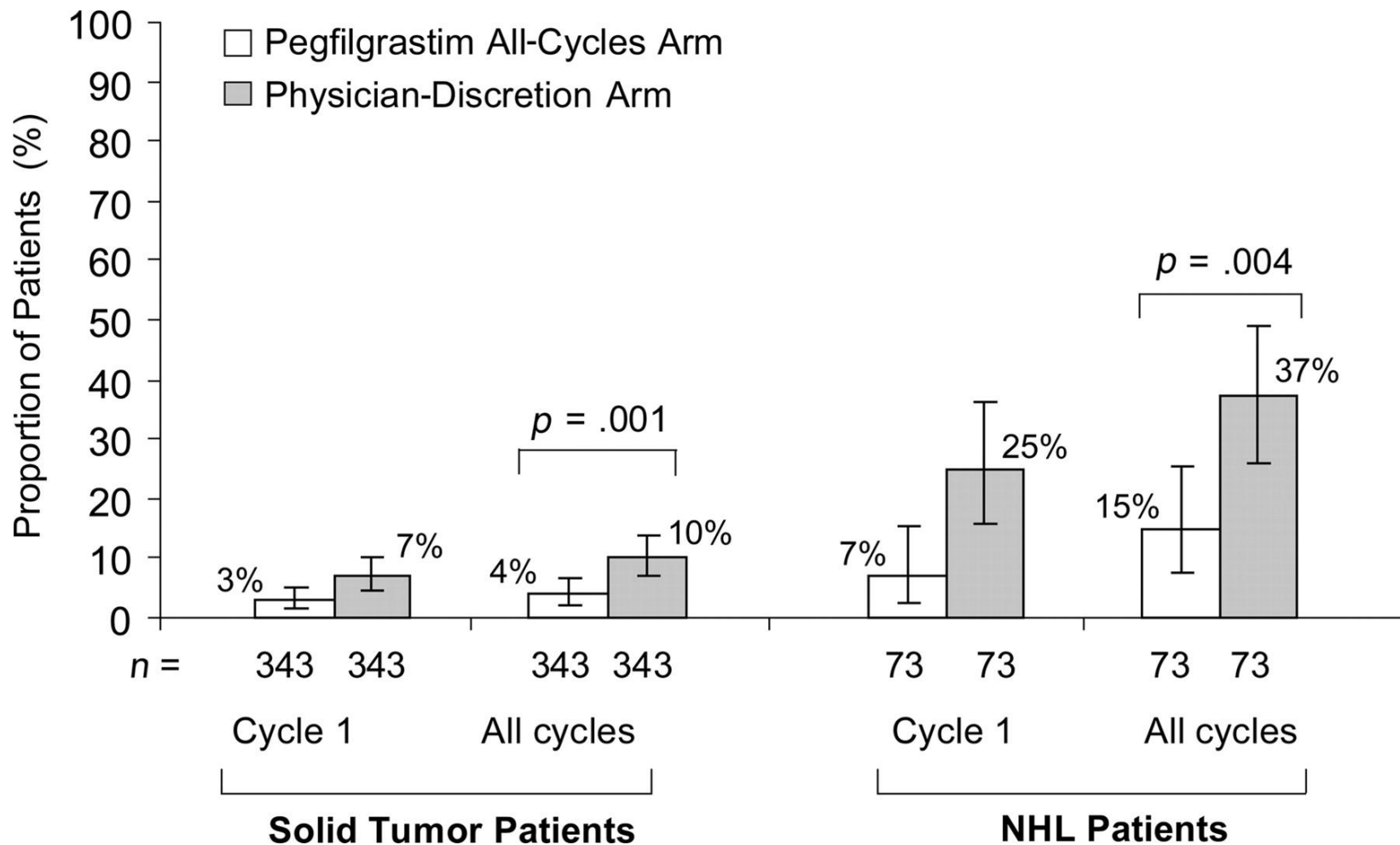
Impact of Reduced RDI on Survival in Elderly DLBCL

N=433 (83 (19.2%) were aged ≥ 70 years). Focus on dose intensity of doxorubicin among elderly patients

The purpose of this study was to analyze the treatment outcomes of elderly patients who were treated with R-CHOP according to the Dose Intensity of Doxorubicin (DID).



Elderly Cancer Patients Receiving Chemotherapy Benefit from Pegfilgrastim Prophylaxis

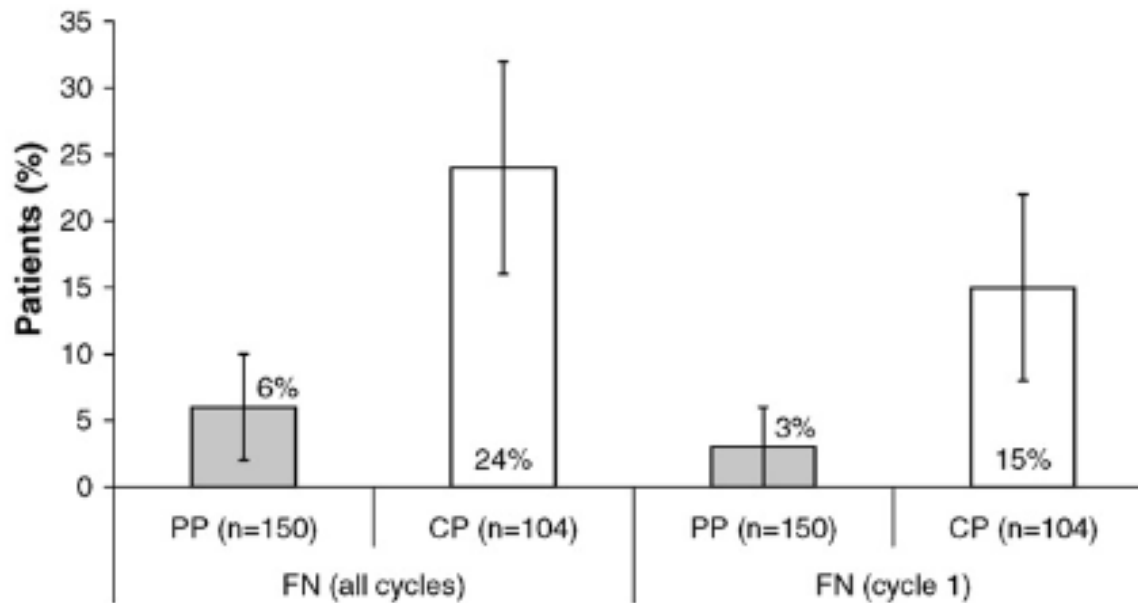


Lodovico Balducci et al. The Oncologist 2007;12:1416-1424

Incidence of FN ($\pm 95\%$ CI) in elderly patients

G-CSF use by elderly patients in the CP cohort in each cycle.

*Daily G-CSF and filgrastim

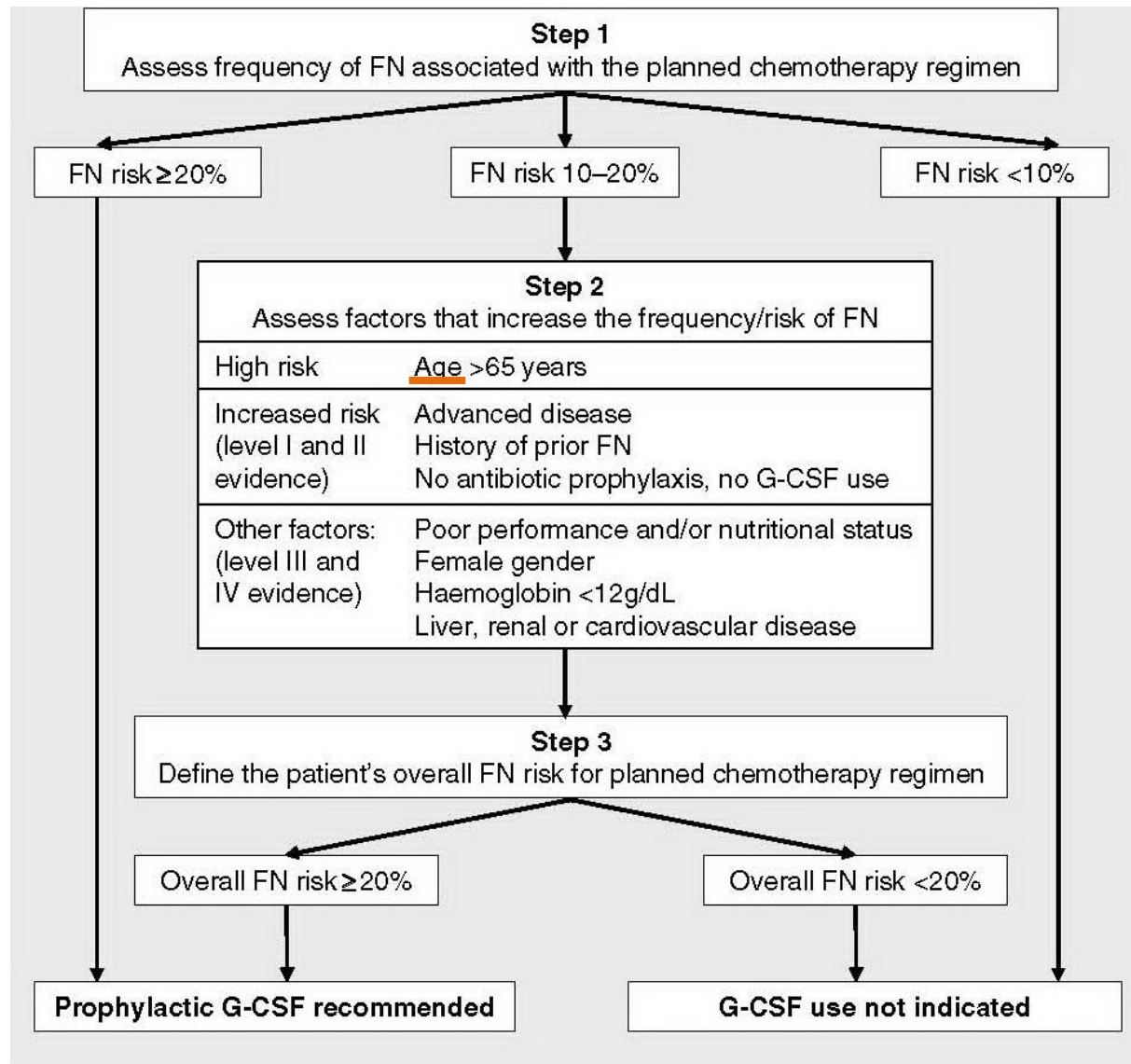


CP, current practice neutropenia management; PP, pegfilgrastim primary prophylaxis

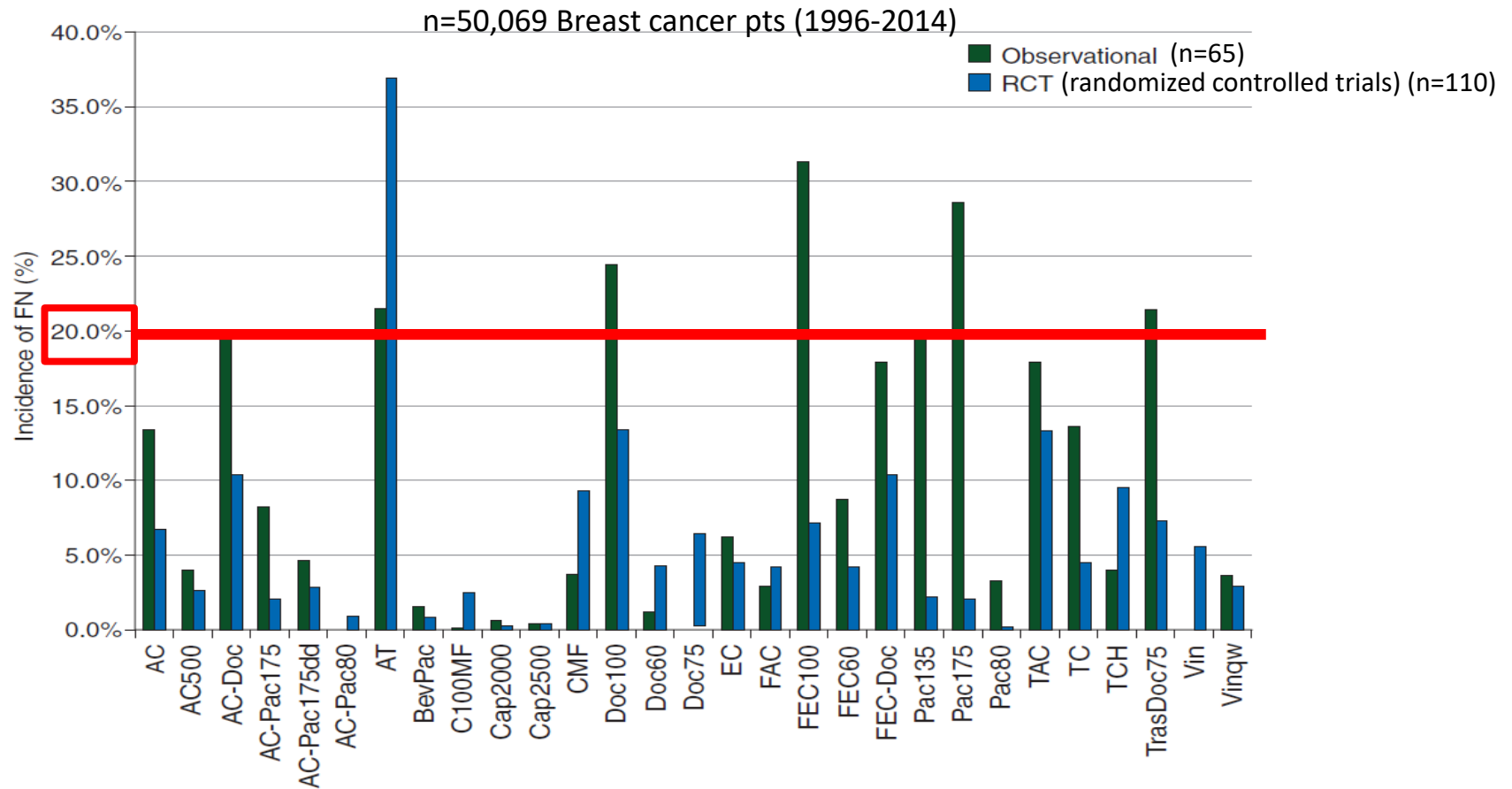
LIPEGFILGRASTIM PROPHYLAXIS IN **ELDERLY** LUNG CANCER PATIENTS RECEIVING CYCLE 1 CHEMOTHERAPY

	≤65-year population		>65-year population	
	Placebo <i>n</i> = 95	Lipegfilgrastim <i>n</i> = 197	Placebo <i>n</i> = 30	Lipegfigrastim <i>n</i> = 53
Incidence of febrile neutropenia <i>n</i> (%)	3 (3.2)	6 (3.0)	4 (13.3)	0

PATIENT ASSESSMENT ALGORITHM TO DECIDE PROPHYLACTIC G-CSF USAGE



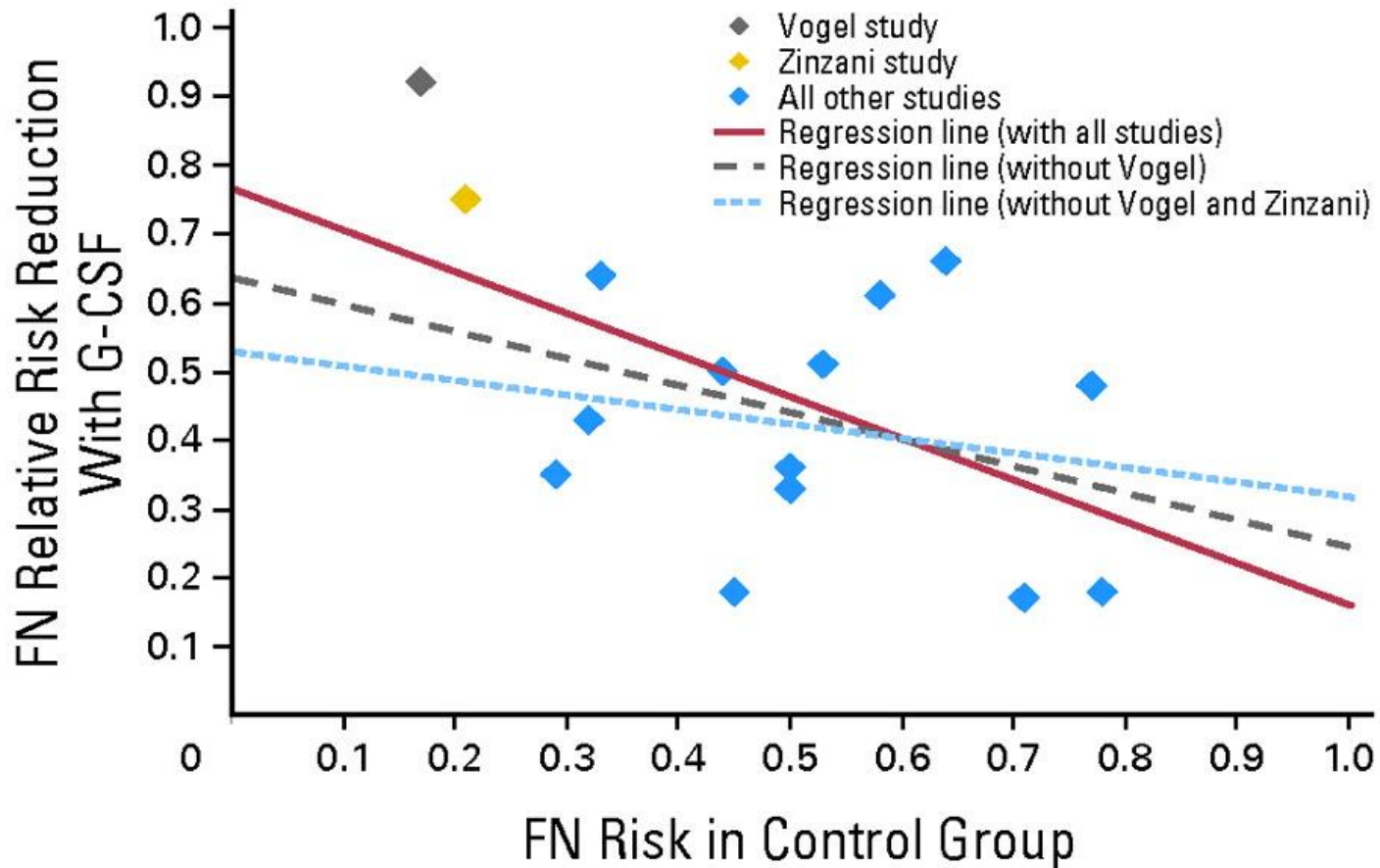
FN Incidence Gap Between Clinical Trials and Real Life Practice



FN rates: significantly higher in the observational study compared with RCT cohorts (OR = 1.74; 95% CI 1.15–2.62; p = 0.012).

This meant that a 13% (95% CI 8.7% to 17.9%) FN rate in RCT would translate into 20% FN rate in observational study.

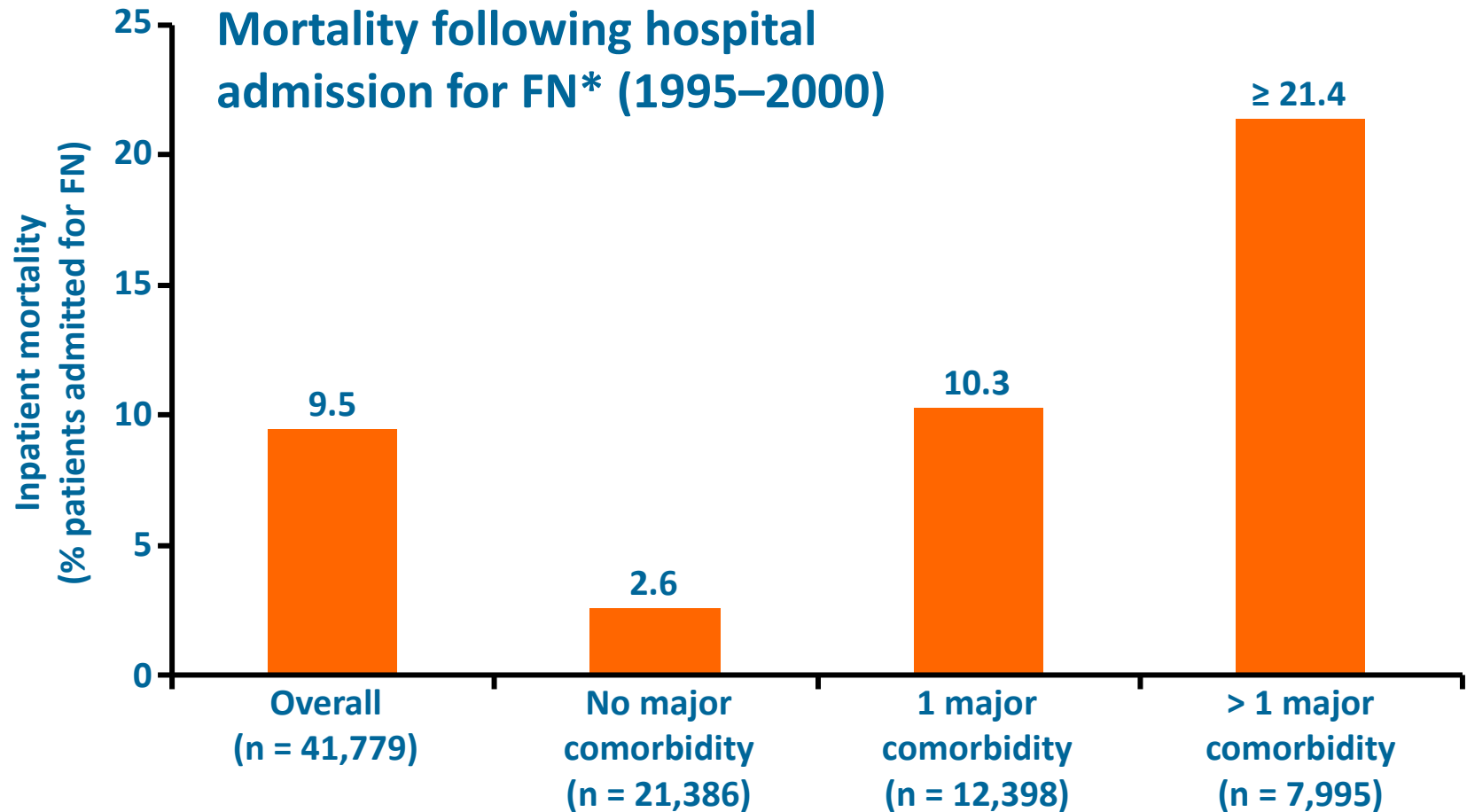
FEBRILE NEUTROPENIA RISK



OVER- AND UNDER-PROPHYLAXIS FOR CHEMOTHERAPY-INDUCED (FEBRILE) NEUTROPENIA

	Under	Correct	Over	
CIN grades 1 through 4	17.9%	16.0%	8.3%	<0.001

RELATIONSHIP BETWEEN FN, RISK OF MORTALITY AND COMORBIDITIES



* Data based on a single admission per patient

BREAKTHROUGH FEBRILE NEUTROPENIA AND ASSOCIATED COMPLICATIONS AMONG **ELDERLY** CANCER PATIENTS RECEIVING MYELOSUPPRESSIVE CHEMOTHERAPY

Baseline demographics and disease characteristics (n=145)

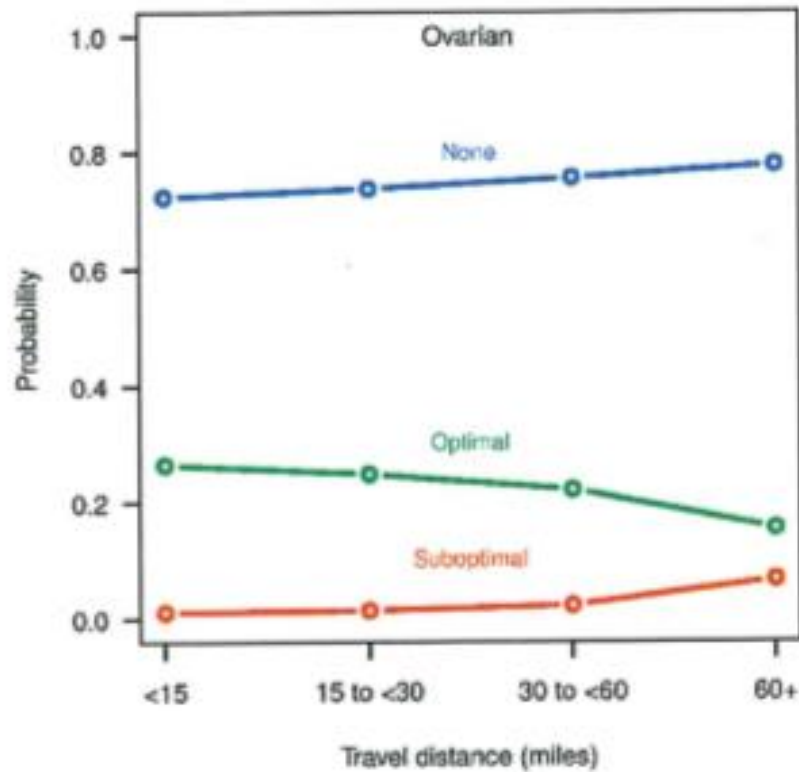
Number of comorbidities	
0	27 (18.6%)
1	42 (29.0%)
≥2	76 (52.4%)

A SINGLE-ARM, RETROSPECTIVE ANALYSIS OF THE INCIDENCE OF FEBRILE NEUTROPENIA USING SAME-DAY VERSUS NEXT-DAY PEGFILGRASTIM

Comparison of study

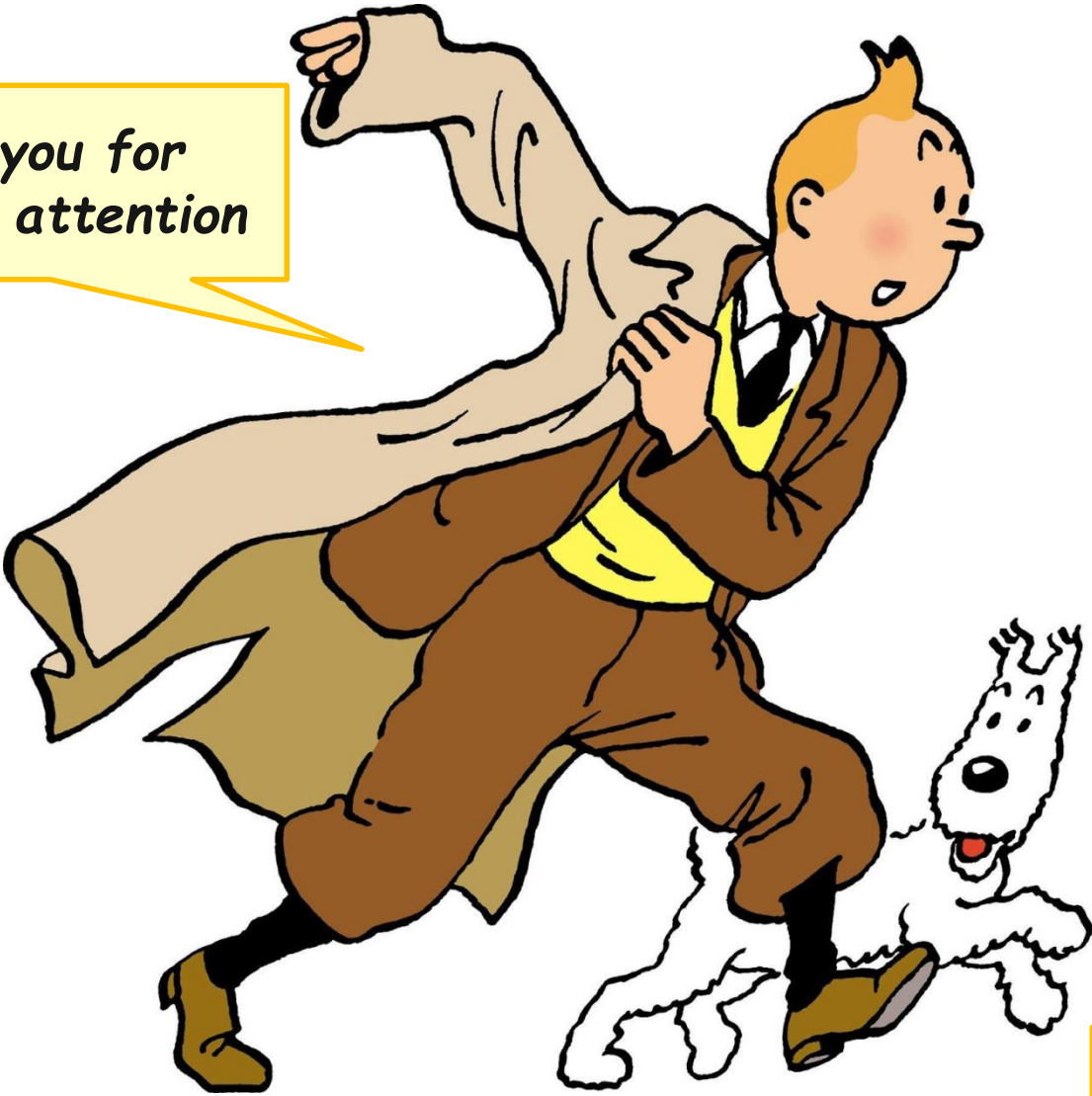
	Hecht et al. (N = 123)	Eckstrom et al. (N = 109)	P value
Grades 3/4 neutropenia	27	13	0.055
Febrile neutropenia	4	4	0.709
Dose delays or dose reductions because of neutropenia or FN	5	11	0.117

ESTIMATED PROBABILITIES OF EACH G-CSF GROUP AS A FUNCTION OF TRAVEL TIME



CONCLUSIONS

- **Age** and co-morbidities (probably inter-related) increase the risk of FN and related complications during chemotherapy
- Primary prophylaxis with G-CSF significantly reduces the risk of FN in **elderly** patients
- Novel approaches for G-CSF administration should be explored in **older** patients (« over » prophylaxis, « same day » administration, biosimilars)



*Thank you for
your kind attention*

See you later !

FN Cumulative risk probability regarding the number of independent risk factors

