

Cancer Associated Thrombosis: Burden of disease

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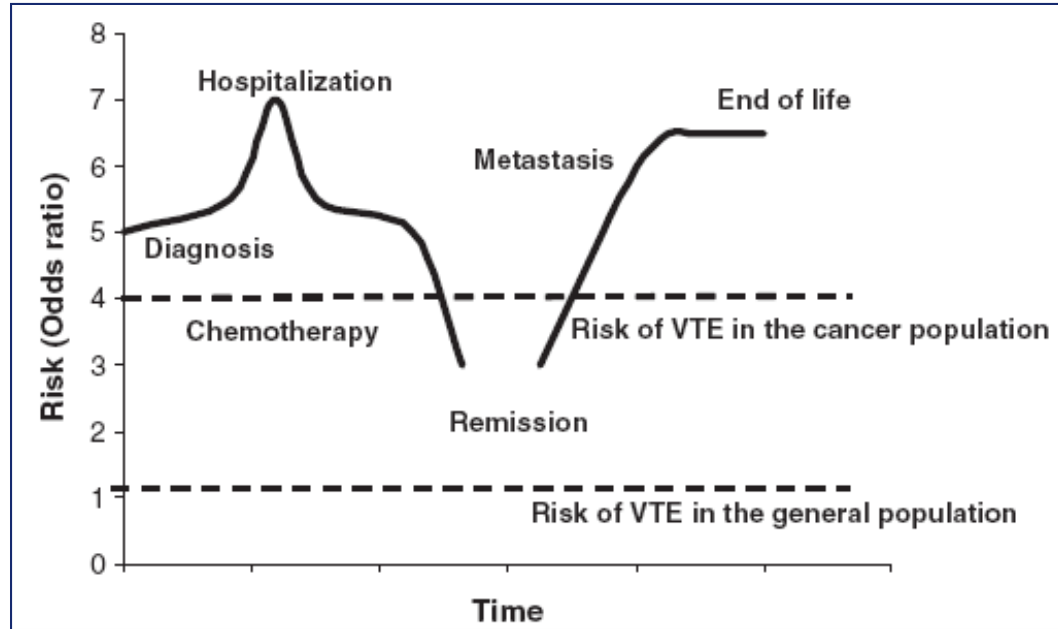
Disclosures

- ◆ Grants and personal fees from Bayer Healthcare
- ◆ Personal fees from: Boehringer-Ingelheim Pharma, Daiichi Sankyo Europe, Sanofi SA, Janssen Pharma

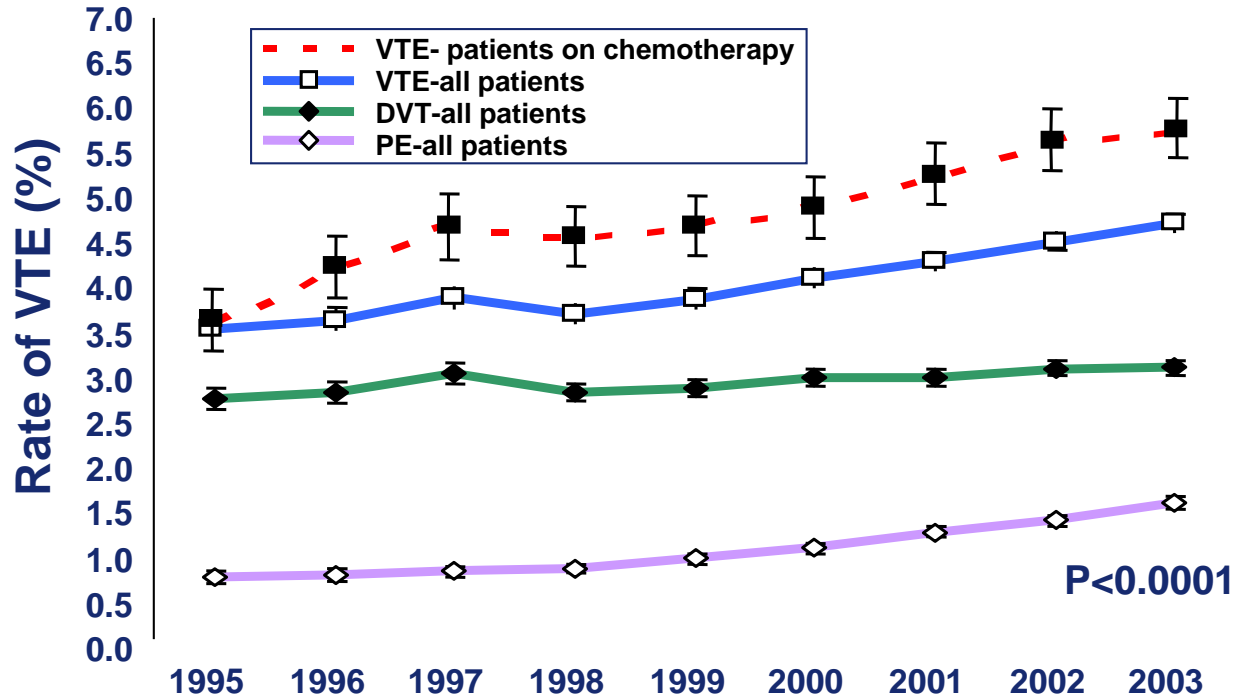
My talk today

- ◆ Incidence
 - Medical oncology
 - Surgical oncology
- ◆ Recurrent VTE
- ◆ Mortality

Risk for VTE varies with natural history of cancer



Trends in VTE in hospitalized cancer patients



ACCP Consensus conference on antithrombotic therapy

Major surgery in cancer patients

	Patients, %
Calf vein	40–80
Proximal vein	10–20
Clinical PE	4–10
Fatal PE	1–5

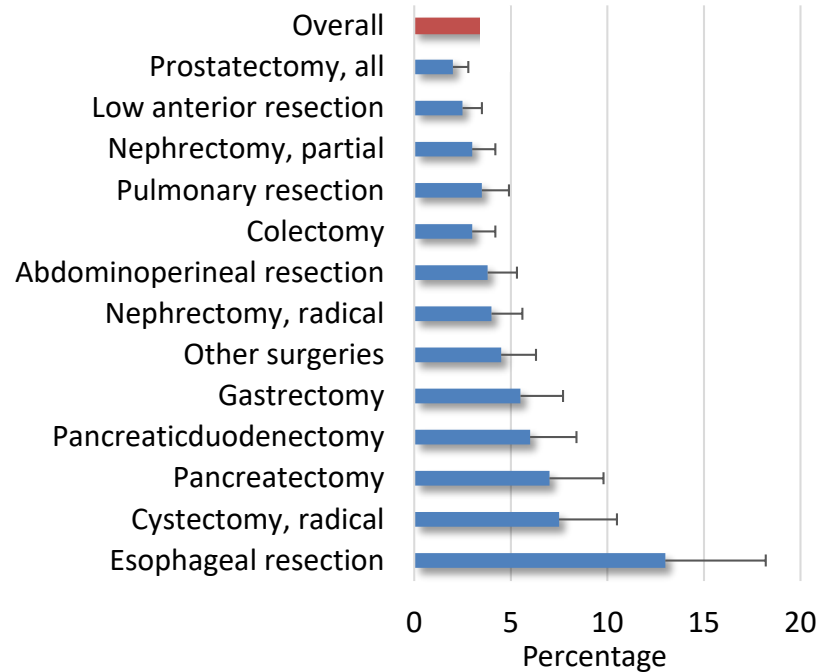
Impact of cancer of postoperative VTE

- ◆ cancer patients have 2-fold risk of post-op DVT/PE and >3-fold risk of fatal PE despite prophylaxis:

	No Cancer N=16,954	Cancer N=6124	P-value
post-op VTE	0.61%	1.26%	<0.0001
non-fatal PE	0.27%	0.54%	<0.0003
autopsy PE	0.11%	0.41%	<0.0001
death	0.71%	3.14%	<0.0001

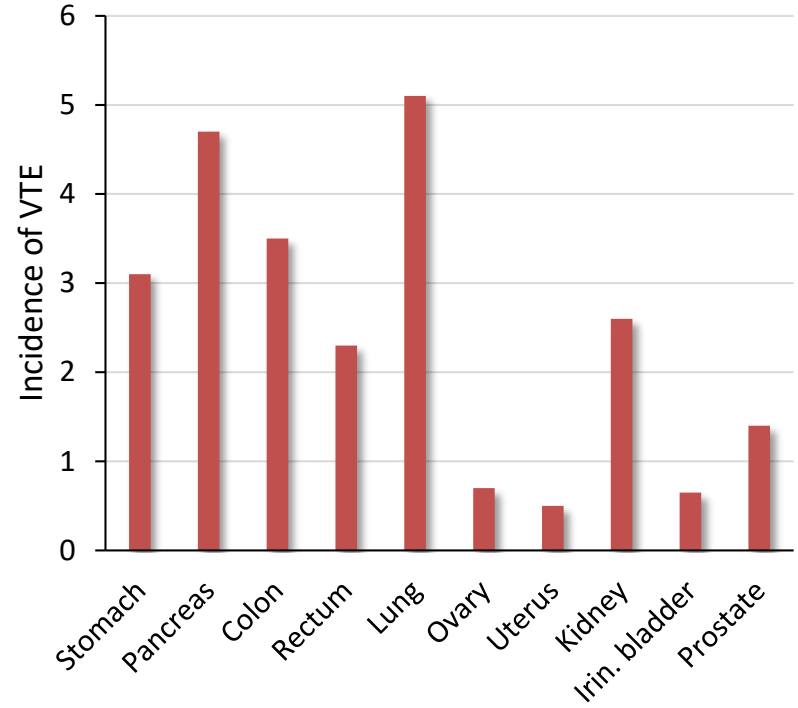
Incidence of VTE after Cancer Surgery

- 20,762 patients undergoing major cancer surgery
- Overall VTE rate 3.5%



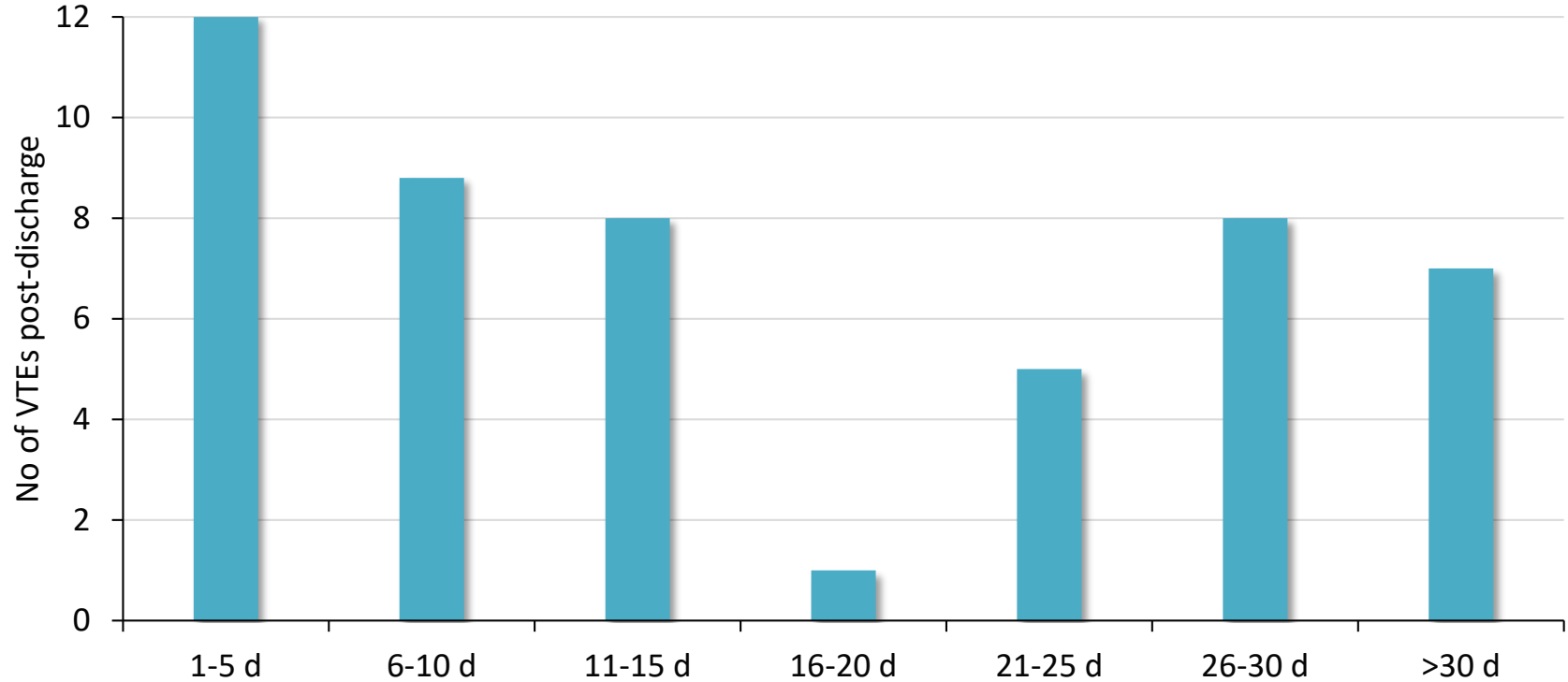
Incidence of VTE-by Site

- Prospective study, 2373 patients undergoing general, urologic, or gynecologic surgery
- Clinical VTE up to 30 days
- Overall incidence = 50 patients (2.1%)





Incidence of VTE - Timing

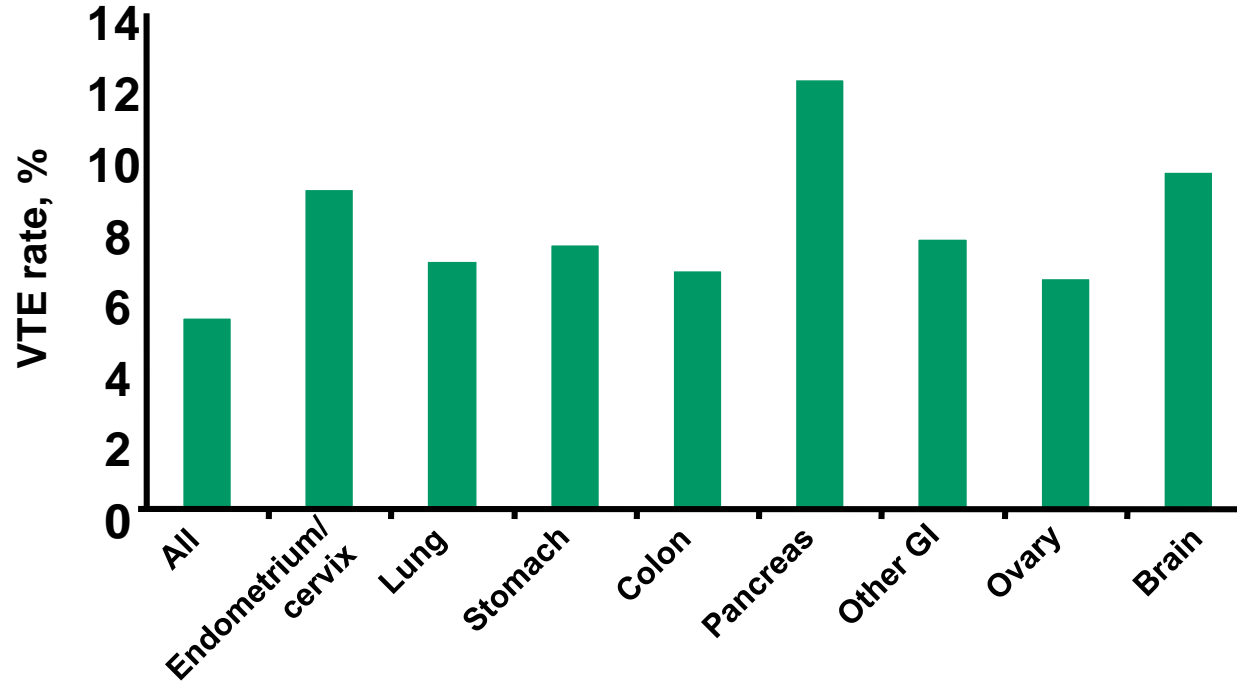


Venous and arterial thrombosis in cancer patients during chemotherapy

	n	Type of cancer	Thrombosis	
			during chemotherapy	after chemotherapy
Weiss, 1981	433	Breast stage II	22 (5%)	0*
Goodnough, 1984	159	Breast stage IV	24 (15%)	4 (2.5%)
Levine, 1988	205	Breast stage II	14 (7%)	0*
Saphner, 1991	2352	Breast	128 (5%)	0*

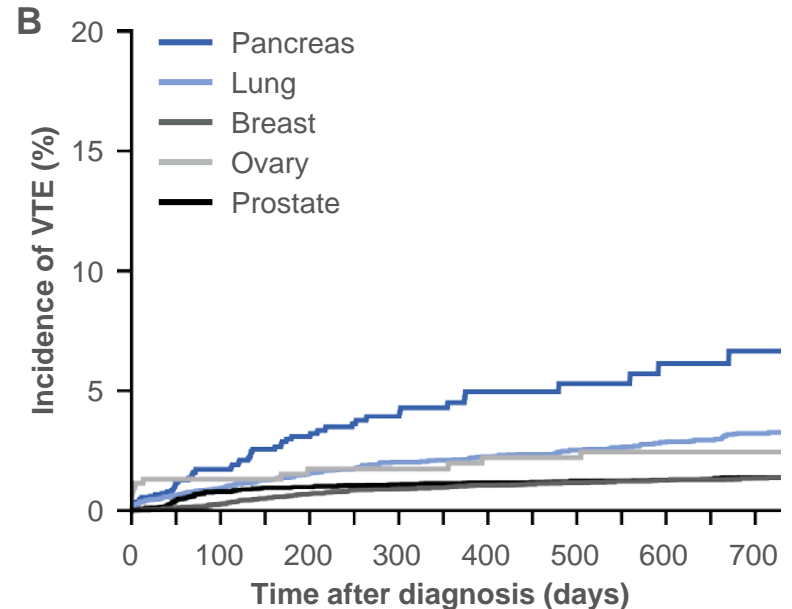
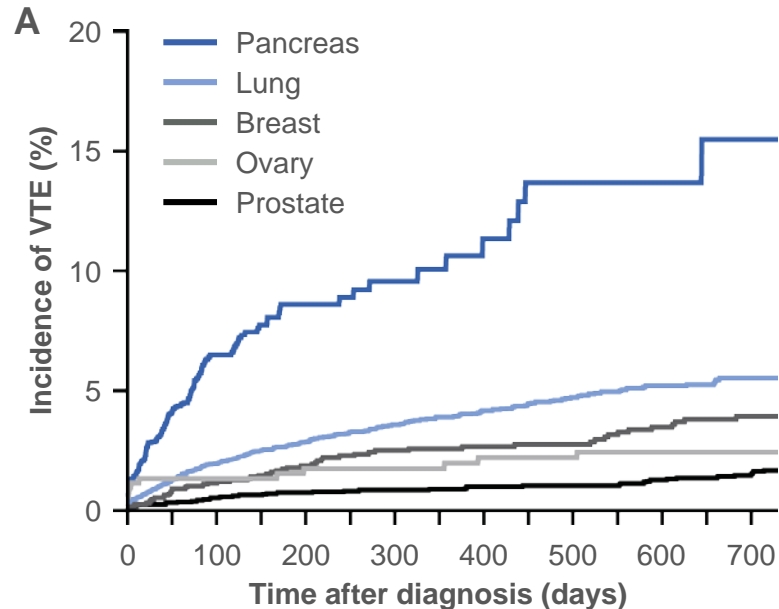
* statistically significant

Risk of inpatient VTE by site/type of cancer



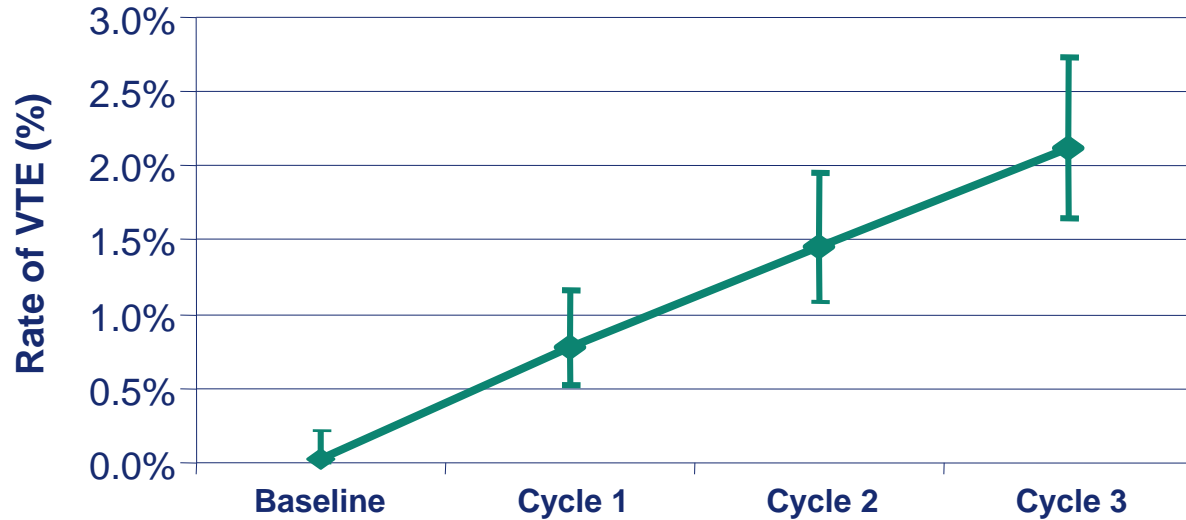
Impact of stage on VTE

Kaplan–Meier plot of the incidence of VTE ≤ 2 years of diagnosis of five different types of cancer with (A) metastatic-stage and (B) regional-stage disease at the time of diagnosis





Incidence of VTE



VTE / 2.4 months	VTE/month	VTE /cycle	Cumulative rate (95% CI)
1.93%	0.8%	0.7%	2.2% (1.7-2.8)

Khorana AA et al. *Cancer*. 2005;104:2822-2829.

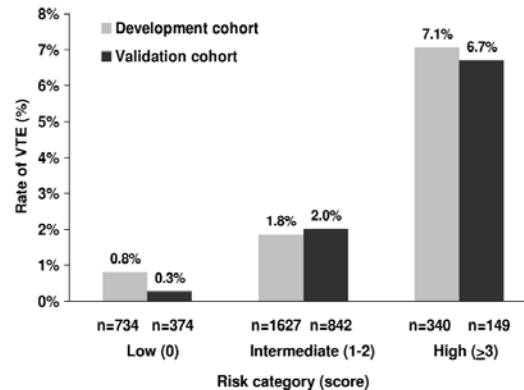
SAVE ONCO Study

	Semuloparin % (n/N)	Placebo % (n/N)	HR (95% CI)	p-value
Overall VTE	1.2 (20/1608)	3.4 (55/1604)	0.36 (0.21–0.60)	<0.001



Identifying patients at risk of VTE

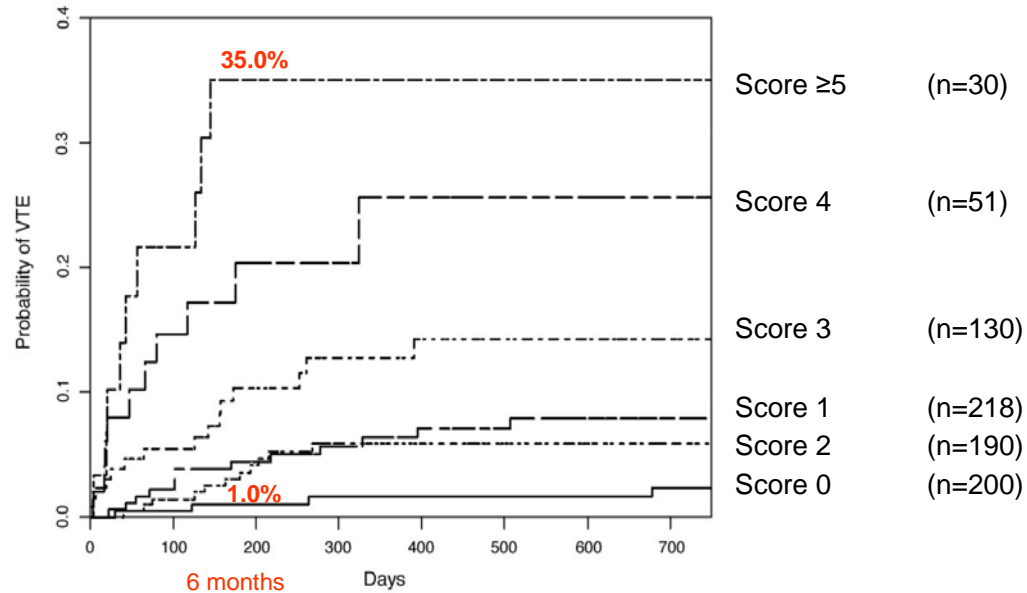
Patient characteristic	β	Odds ratio* (95% CI)
Site of cancer		
Very high risk (stomach, pancreas)	1.46	4.3 (1.2-15.6)
High risk (lung, lymphoma, gynecologic, genitourinary excluding prostate)	0.43	1.5 (0.9-2.7)
Low risk (breast, colorectal, head and neck)	0.0	1.0 (reference)
Prechemotherapy platelet count $350 \times 10^9/L$ or more	0.60	1.8 (1.1-3.2)
Hemoglobin level less than 100 g/L or use of red cell growth factors	0.89	2.4 (1.4-4.2)
Prechemotherapy leukocyte count more than $11 \times 10^9/L$	0.77	2.2 (1.2-4)
BMI 35 kg/m^2 or more	0.90	2.5 (1.3-4.7)





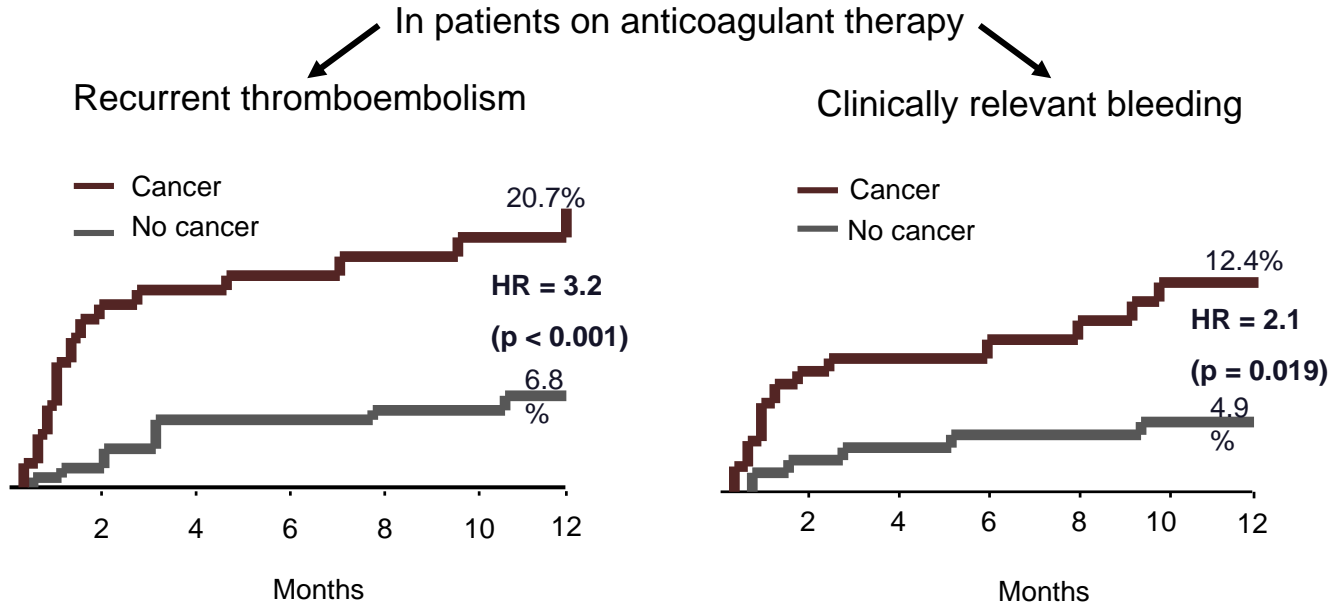
The Vienna CATS score

- Khorana score plus biomarkers (D-dimer and sP-selectin)



VTE treatment in cancer patients

Benefit and risk balance more difficult to achieve



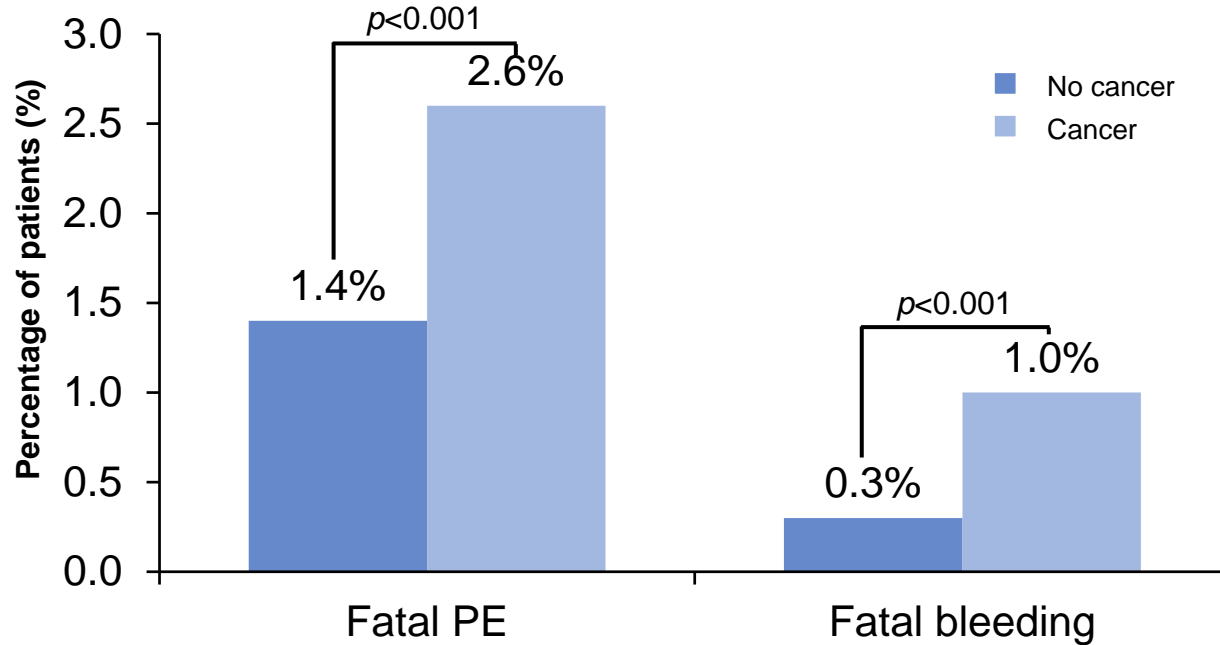
Incidence of central venous catheters (CVC)-related DVT without prophylaxis

	ENDPOINT	TOTAL DVT
Lokich, 1983	Venography	42.0%
Bern, 1990	Venography	37.0%
Monreal, 1996	Venography	61.7%
Verso, 2005	Venography	18.0%
Luciani, 2001	Doppler US	11.8%
Couban, 2005	Clinical	4.0%
Reichardt, 2002	Clinical	4.0%
Karthaus, 2005	Clinical	3.4%
Lee, 2006	Clinical	4.3%



Higher rates of fatal PE and fatal bleeding in patients with cancer

Risk of fatal PE or fatal bleeding in the RIETE registry¹



1. Monreal M *et al. J Thromb Haemost* 2006;4:1950–1956



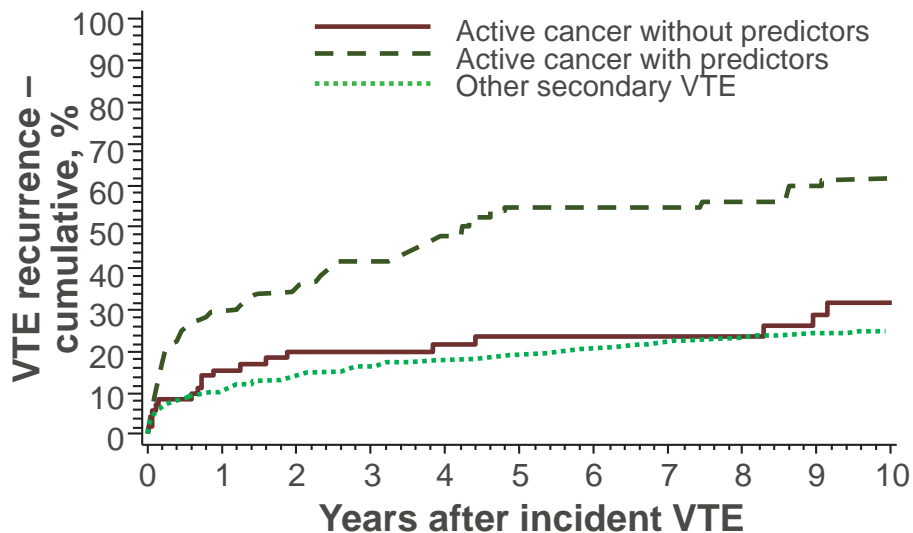
Recurrent Thrombosis and Bleeding Events

INR range	Recurrent VTE		Major Bleeding	
	Cancer	No Cancer	Cancer	No Cancer
< 2.0	54.0	15.9	30.6	0.0
2.0 to 3.0	18.9	7.2	11.2	0.8
> 3.0	18.4	6.4	0.0	6.3
Overall	27	9	13.3	2.1

Hutten et al. J Clin Oncol 2000;18:3078.

Predicting VTE Recurrence

Cumulative incidence of first VTE recurrence



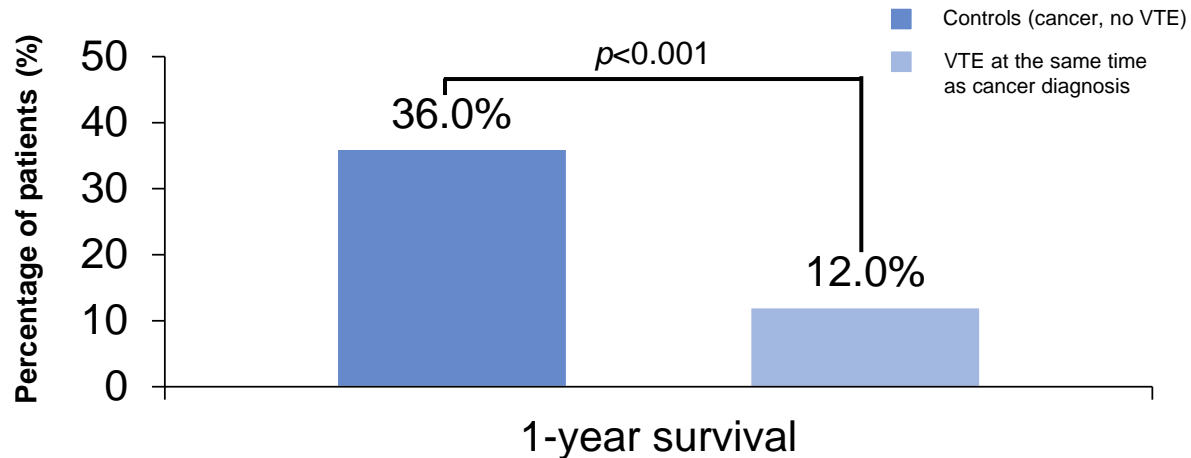
Multivariate predictors of VTE recurrence

Characteristic	HR	95% CI	p-value
Stage IV pancreatic cancer	6.38	2.69–15.13	<0.0001
Brain cancer	4.57	2.07–10.09	0.0002
Myeloproliferative or myelodysplastic disorder	3.49	1.59–7.68	0.002
Ovarian cancer	3.22	1.57–6.59	0.001
Stage IV cancer (non-pancreas)	2.85	1.74–4.67	<0.0001
Lung cancer	2.73	1.63–4.55	0.0001
Neurological disease with leg paresis	2.38	1.14–4.97	0.02
Cancer stage progression	2.14	1.30–3.52	0.003
Warfarin therapy	0.43	0.28–0.66	<0.0001



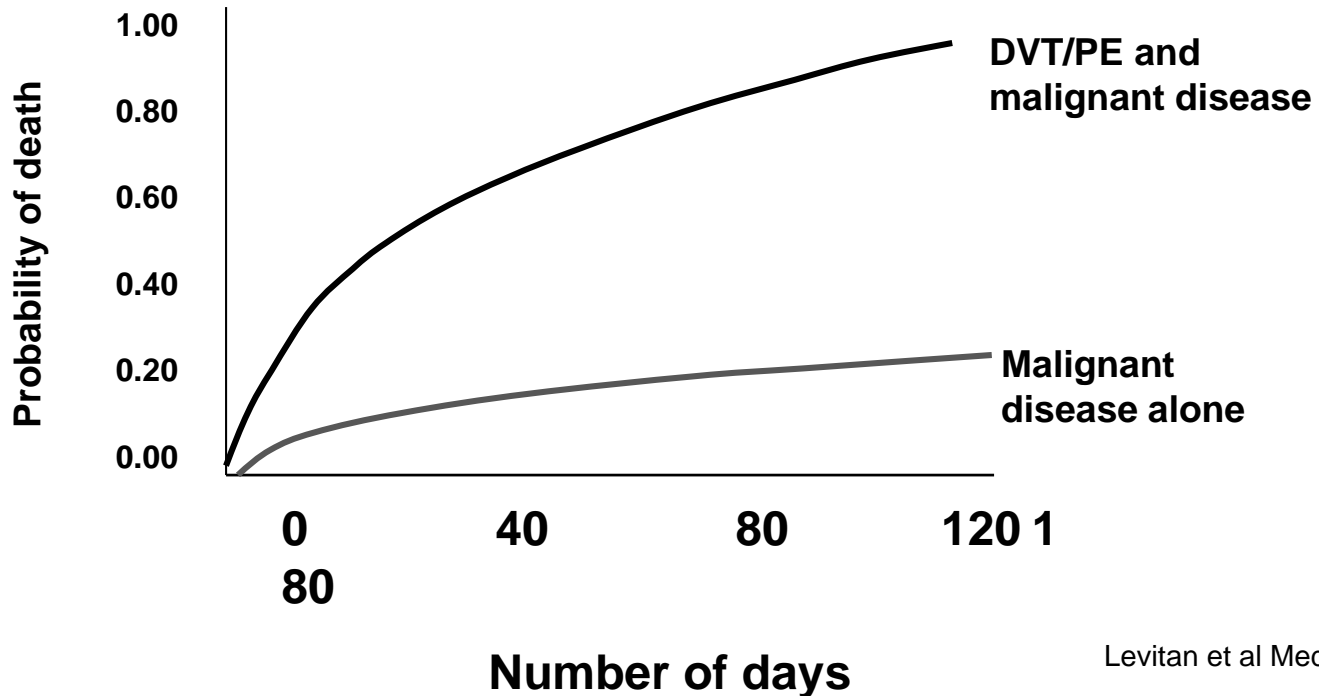
Cancer and VTE predict poor outcome

- ◆ Patients with a diagnosis of cancer at the time of an episode of VTE were more likely to have distant metastases and had poorer 1-year survival than matched controls with cancer but no VTE

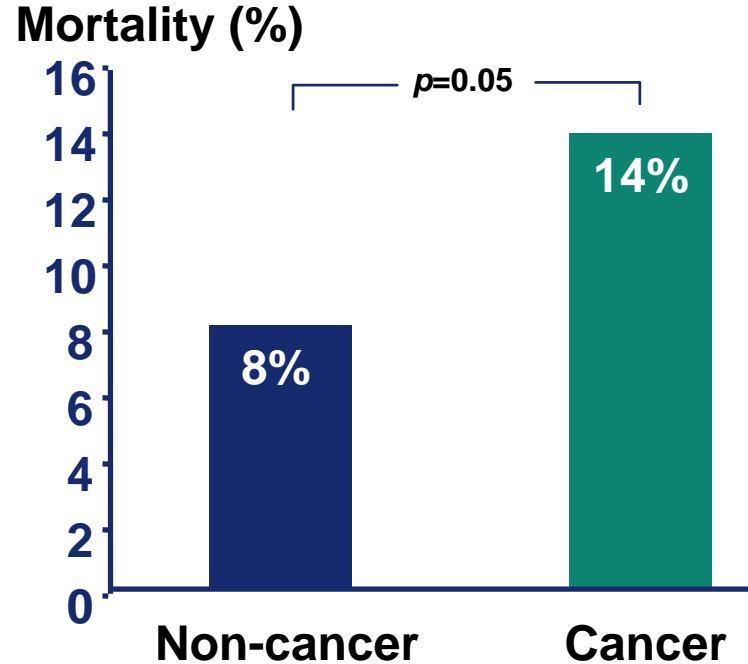


Concurrent VTE and cancer increases the risk of death

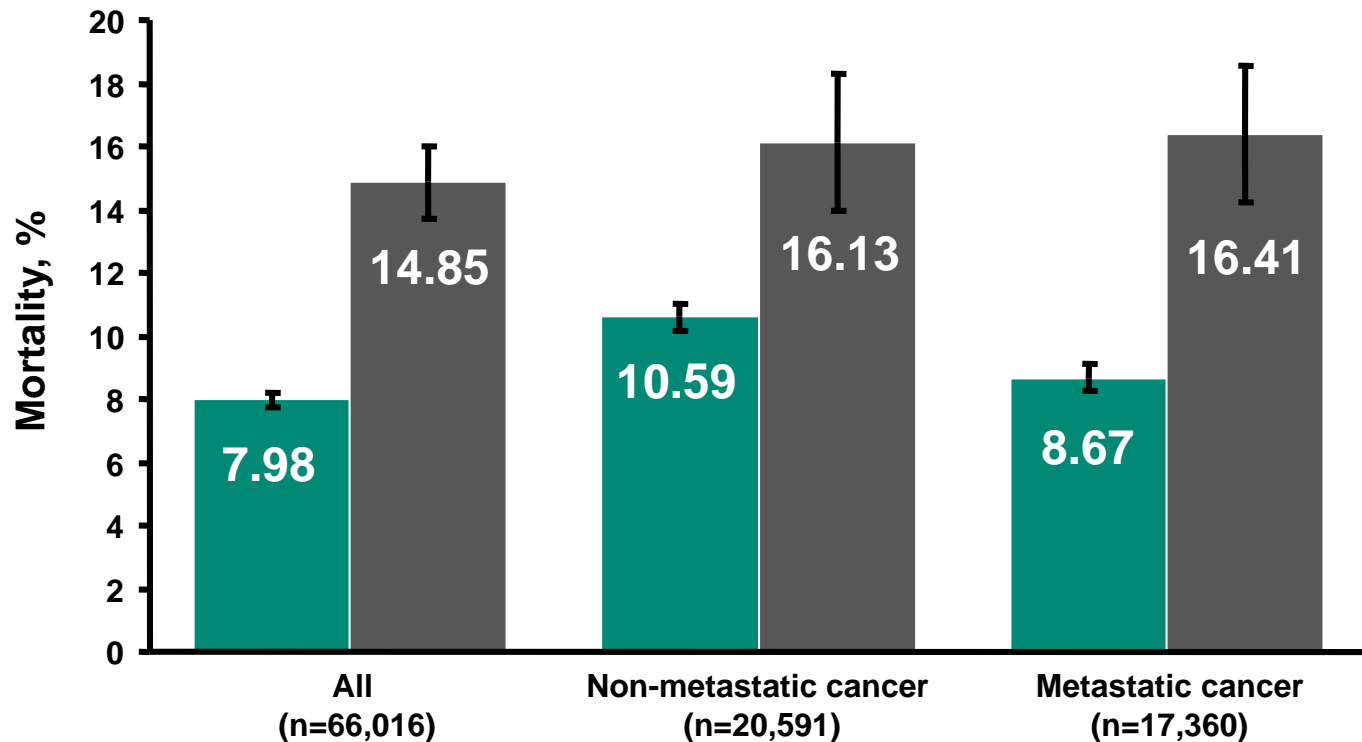
Probability of death within 183 days of initial hospital admission



In hospital mortality rate due to pulmonary embolism (PE)



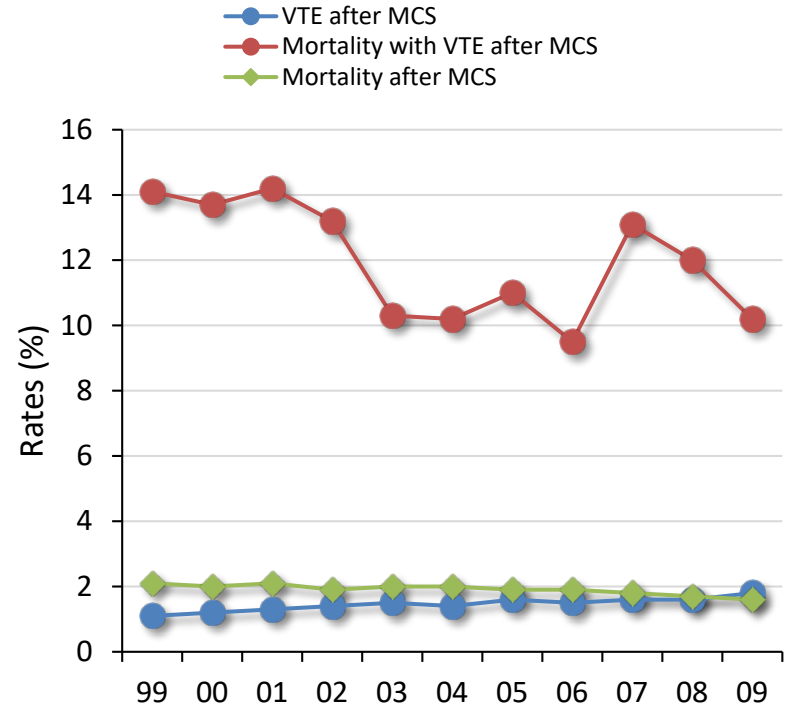
VTE and in-patient mortality





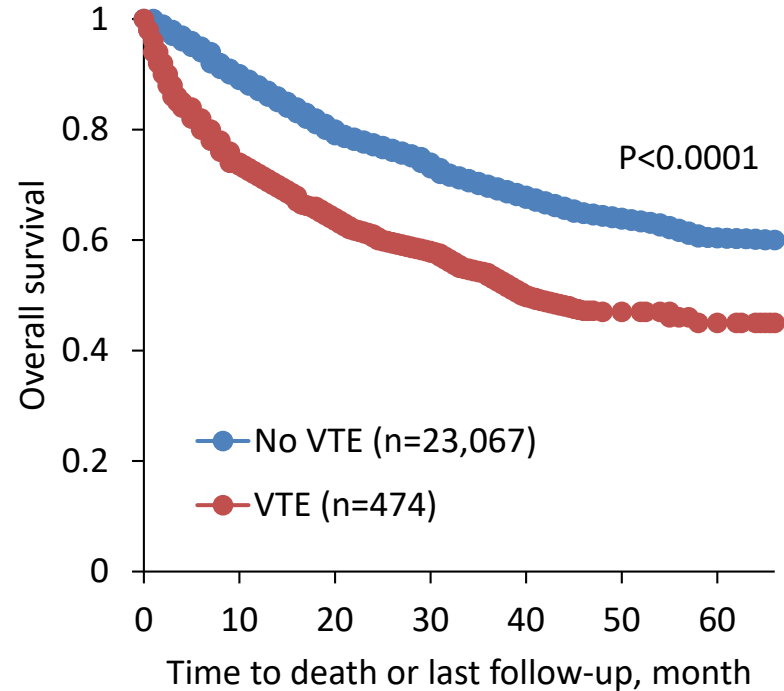
Impact of VTE on Mortality

- Nationwide Inpatient Sample 1999-2009
- N = 2,508,916



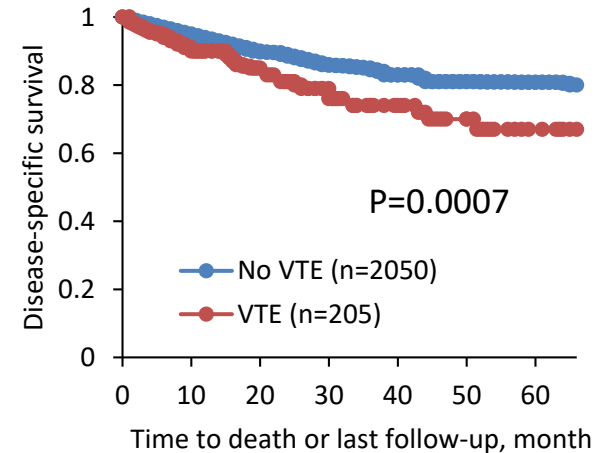
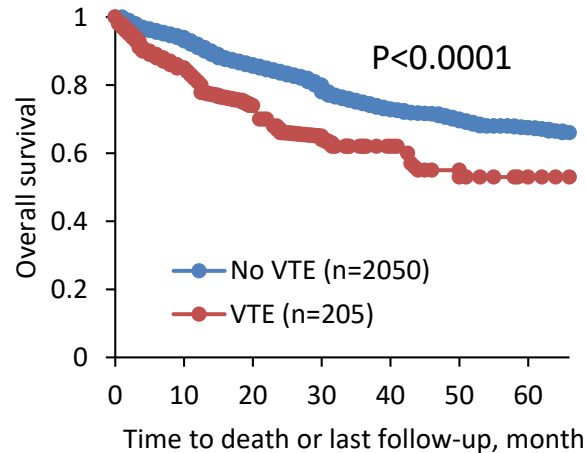
Postoperative VTE and Survival

- 23,541 patients having cancer surgery
- 474 (2%) VTEs
- 5 year OS 43.8% vs 61.2%



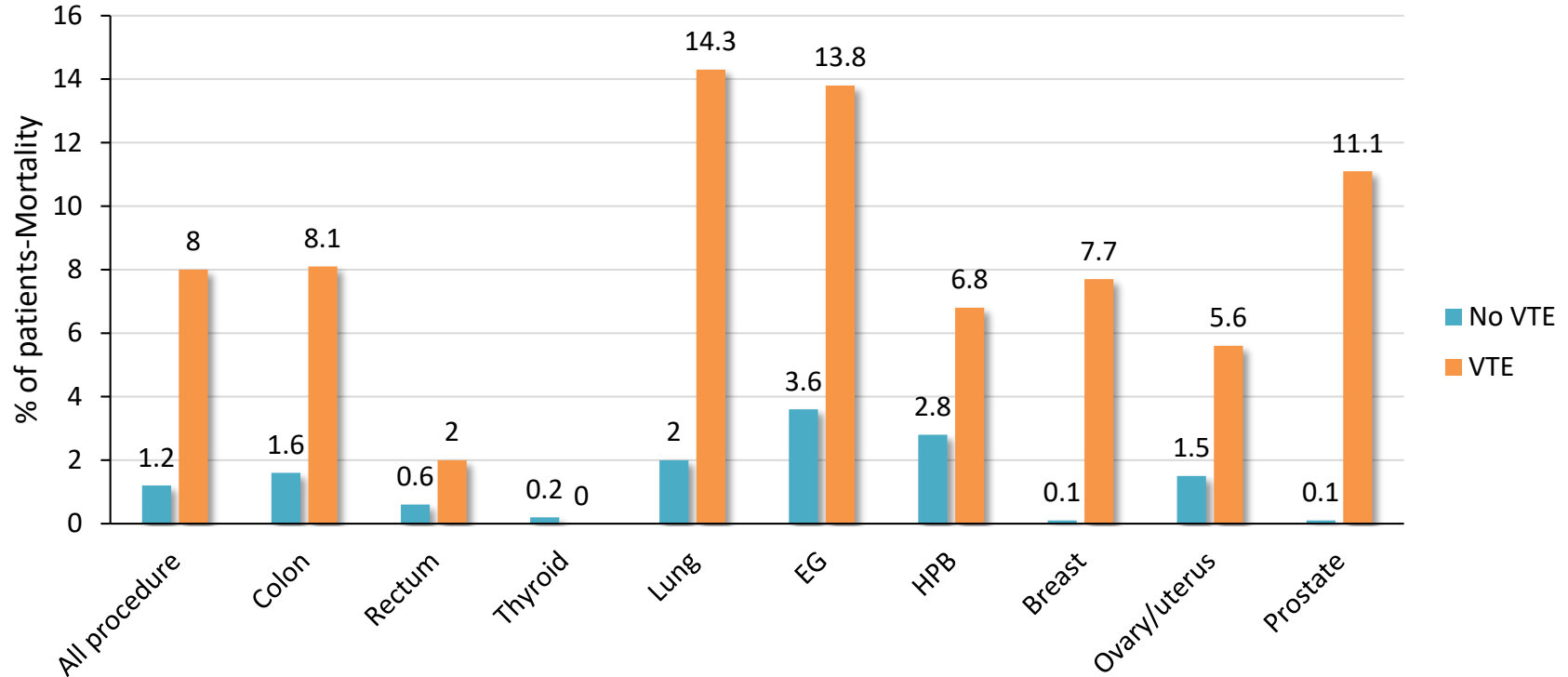
Postoperative VTE and Survival

- Matched for:
 - Gender
 - Age
 - Year of surgery
 - Type of cancer
 - Stage
 - Procedure



- Worse DSS in patients with VTE

Impact of VTE on outcome



Conclusion

- ◆ Cancer is an important risk factor for VTE
- ◆ Impact on medical and surgical cancer patients
- ◆ Attended by higher risk for bleeding and recurrence
- ◆ Impacts mortality