

Epidemiologia del tromboembolismo venoso nel paziente oncologico

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Varese

Thromboembolism in Patients with Cancer

- **Venous thromboembolism (VTE) is the second most frequent, potentially fatal, complication in cancer patients, affecting approximately 1 in 200 cancer patients (Cunningham 2006)**
- **15% of patients with cancer present an episode of venous thromboembolism throughout their disease (Rickles 1998)**
- **10% of patients with unprovoked VTE develop a cancer in the 2 years following the index event (Prandoni 1996)**

Prevalence of cancer in patients with VTE: MASTER registry

Age groups

Known cancer

Newly diagnosed cancer

Transient risk factors

	<40y	41-60	61-80	>80
Known cancer	5.2%	17.8%	24.5%	15.2%
Newly diagnosed cancer	0.7%	2.1%	2.4%	5.8%
Transient risk factors	58.7%	38.6%	36.3%	46.6%

Cancer and VTE risk

The exact incidence of VTE in patients with cancer is unknown

Confounding factors:

heterogeneity of cancer population

heterogeneity of CHT regimens

comorbidities

surgery, CVC, invasive procedures

Factors associated with the risk of thrombosis: MEGA study

3220 Patients with first episode of VTE

	OR (95%CI)
Cancer/ non cancer	6.7 (5.2-8.6)
Hematological cancer	28.0 (4.0- 199)
Lung cancer	22.2 (3.6-136.1)
GI cancer	20.3 (4.9-83.0)
< 6 months after cr diagnosis	53.5 (8.6-334.3)
Metastatic cancer	19.8 (2.6-149.1)

Incidence of VTE < 1 yr of the cancer diagnosis

528,693 cancer patients

SIR 1.3 (95%CI; 1.2-1.5; P <0.001)

Elevated SIR (range 1.8-4.2)

Pancreatic cancer

Stomach cancer

Lung cancer

Acute myelogenous leukemia

Non-Hodgkin lymphoma

Renal cell cancer

Ovarian cancer

SIR for metastatic cancer: 2.3 (95%CI; 2.0-2.6) P <0.001

Incidence of Venous Thromboembolism and Its Effect on Survival Among Patients With Common Cancers

Arch Intern Med. 2006;166:458-464

Helen K. Chew, MD; Theodore Wun, MD; Danielle Harvey, PhD; Hong Zhou, PhD; Richard H. White, MD

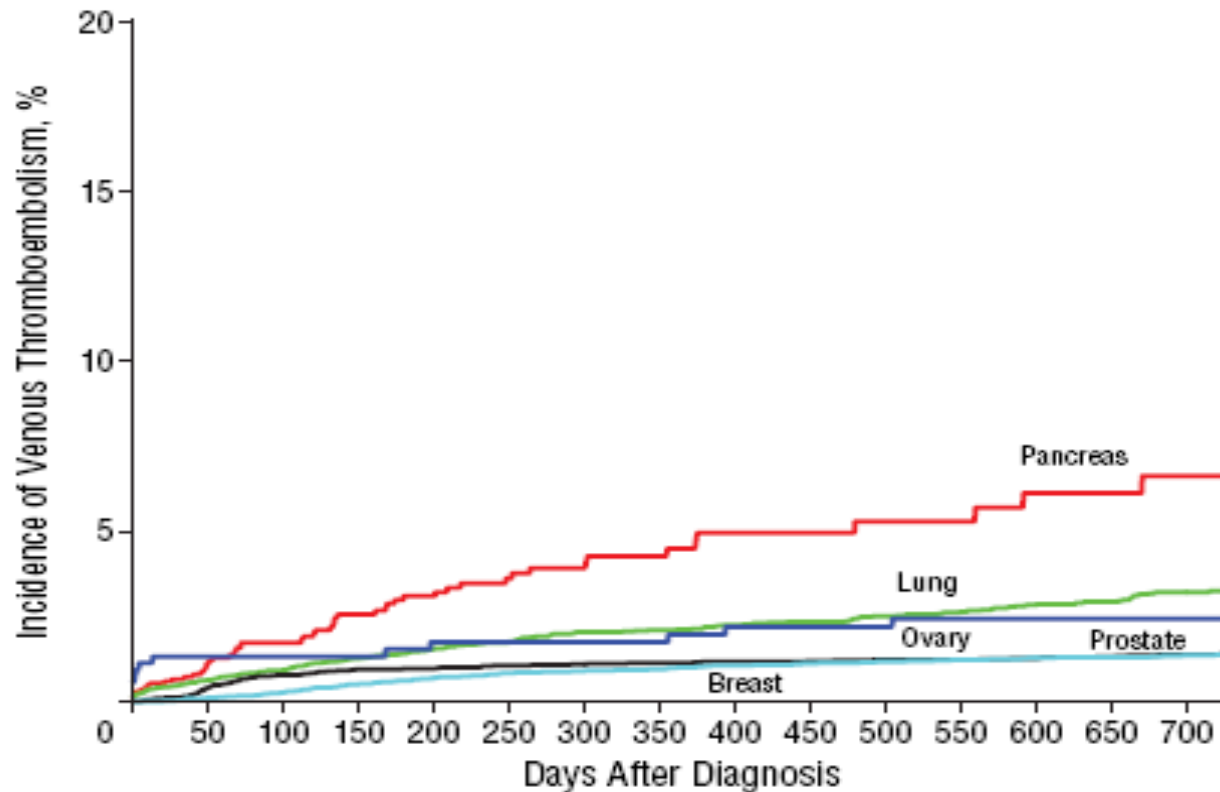


Figure 2. Kaplan-Meier plot of the incidence of venous thromboembolism within 2 years of diagnosis of 5 different types of cancer with regional-stage disease at the time of diagnosis.

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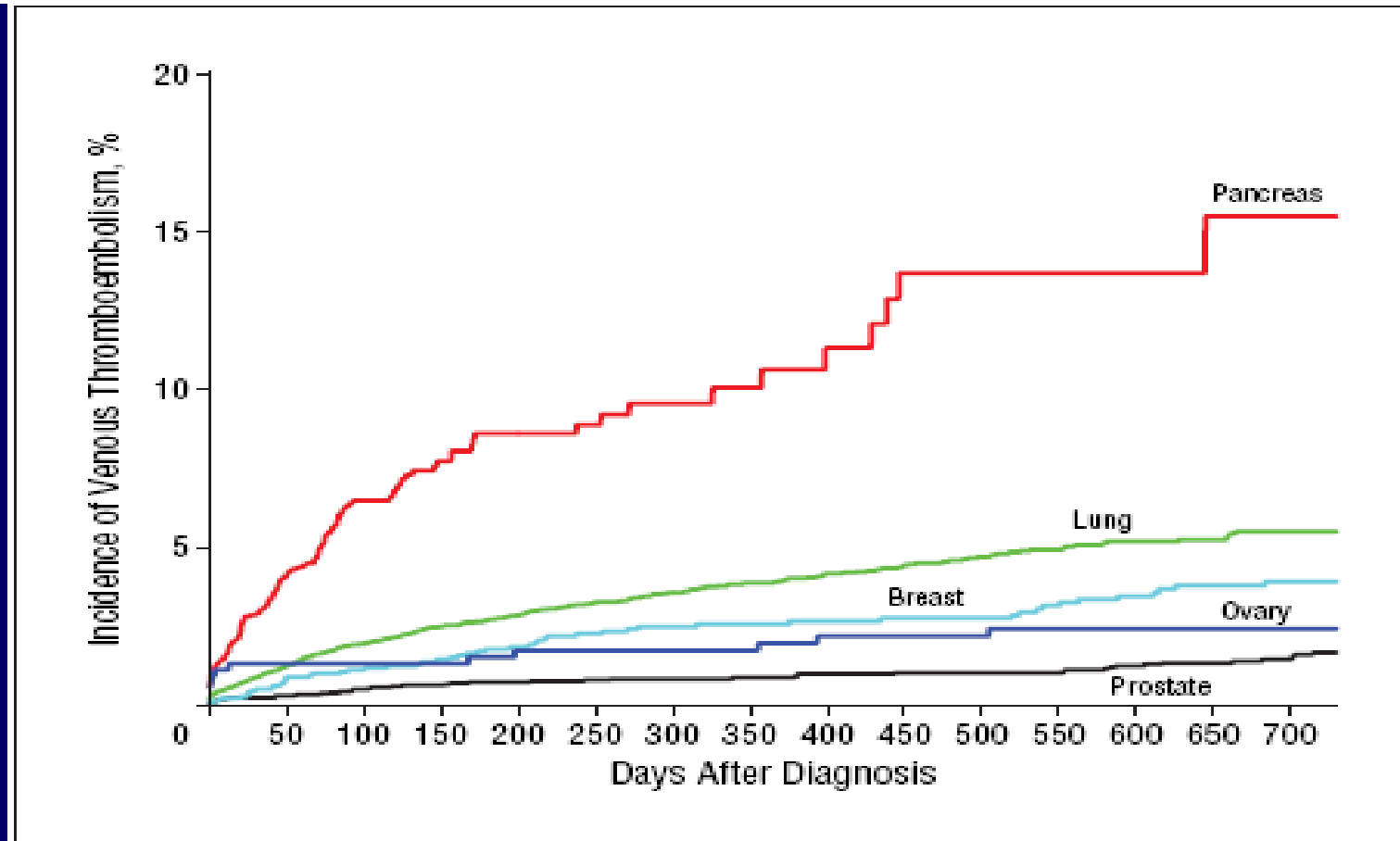


Figure 1. Kaplan-Meier plot of the incidence of venous thromboembolism within 2 years of diagnosis of 5 different types of cancer with metastatic-stage disease at the time of diagnosis.

The risk of a venous thrombotic event in lung cancer patients: higher risk for adenocarcinoma than squamous cell carcinoma

Journal of Thrombosis and Haemostasis, 2: 1760–1765

J. W. BLOM, * S. OSANTO† and F. R. ROSENDAAL *†

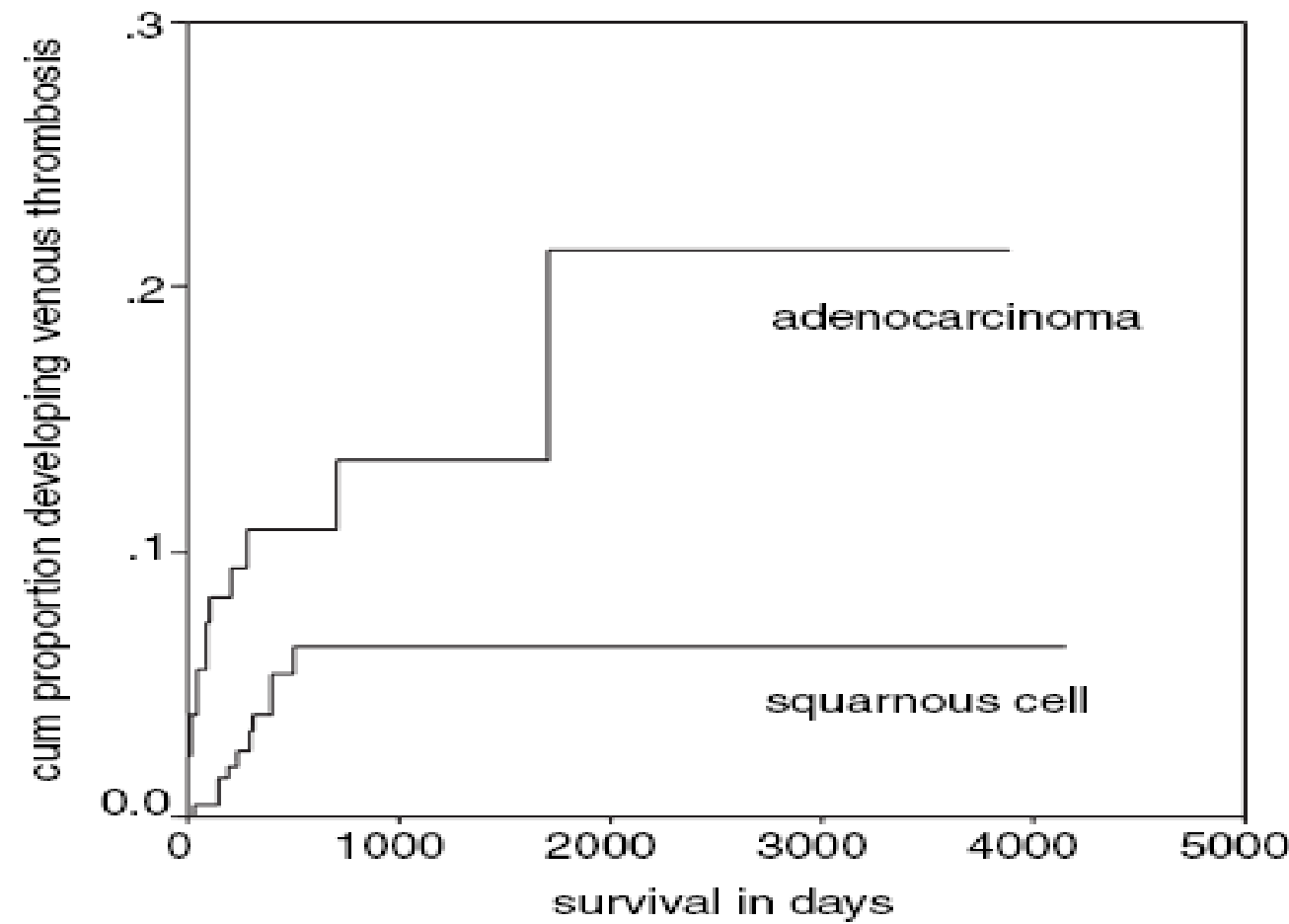


Fig. 1. Cumulative proportion of venous thrombosis in patients with a squamous cell carcinoma vs. patients with an adenocarcinoma.

The risk of postoperative DVT is increased after general surgery for cancer

	Cancer patients	Non-cancer patients
Kakkar et al. 1970	24/59 (41%)	38/144 (26%)
Hills et al. 1972	8/16 (50%)	7/34 (21%)
Walsh et al. 1974	16/45 (35%)	22/217 (10%)
Rosenberg et al. 1975	28/66 (42%)	29/128 (23%)
Sue-Ling et al. 1986	12/23 (52%)	16/62 (26%)
Allan et al. 1983	31/100 (31%)	21/100 (21%)
Multicenter Trial 1984	9/37 (22%)	13/53 (24%)
All	128/346 (37%)	146/738 (20%)

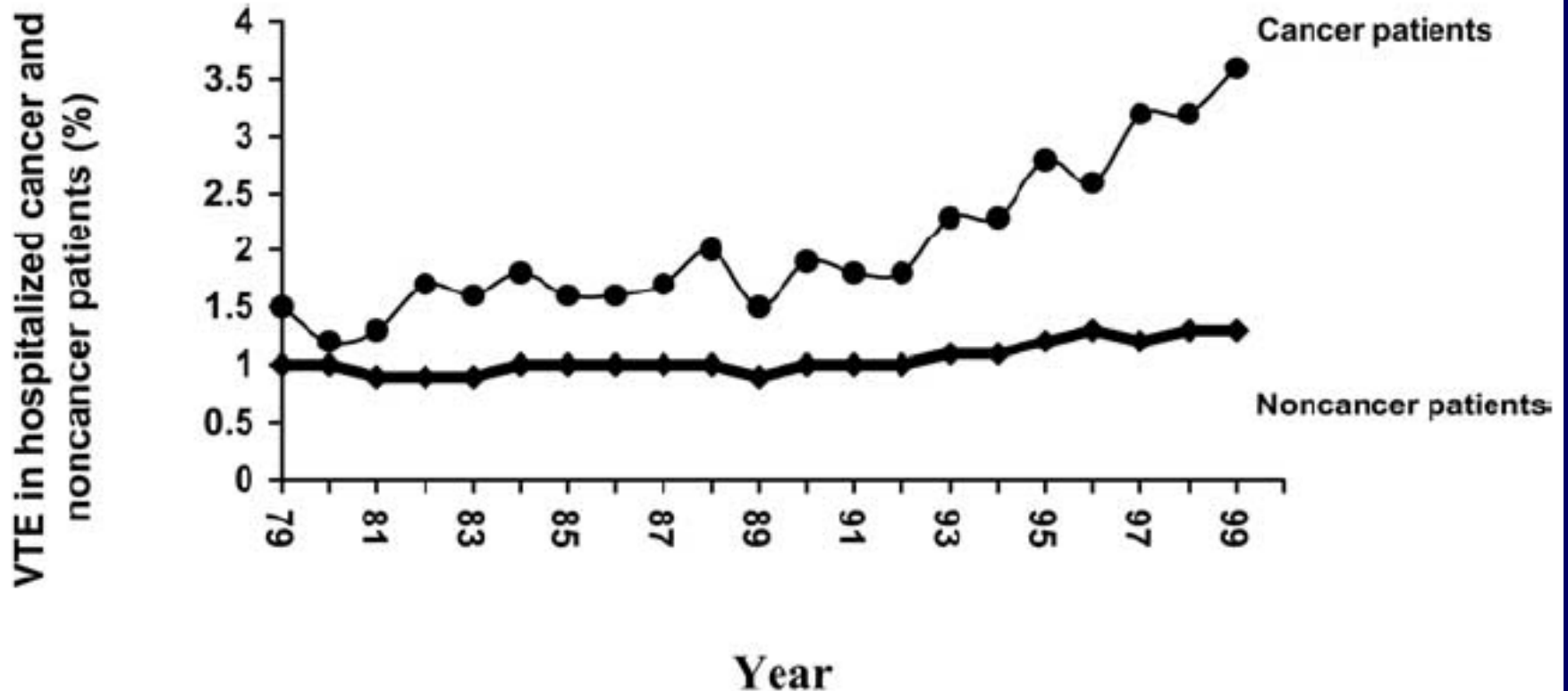
Incidence of symptomatic VTE in cancer surgery: @RISTOS project

- **Symptomatic VTE (up to day 35): 2.1%**
 - **General surgery: 2.8%**
 - **Gynecology: 2.0%**
 - **Urology: 0.9%**
- **Death rate: 1.7% (46.3% caused by VTE)**

Mean time	17.2 ± 14.0 days
Time (range)	2-58 days
Events after >21 days	40%

Incidence of Venous Thromboembolism in Patients Hospitalized with Cancer

Paul D. Stein, MD,^{a,b} Afzal Beemath, MD,^a Frederick A. Meyers, MD,^c Elias Skaf, MD,^a Julia Sanchez, MD,^a Ronald E. Olson, PhD^d
The American Journal of Medicine (2006) 119, 60-68



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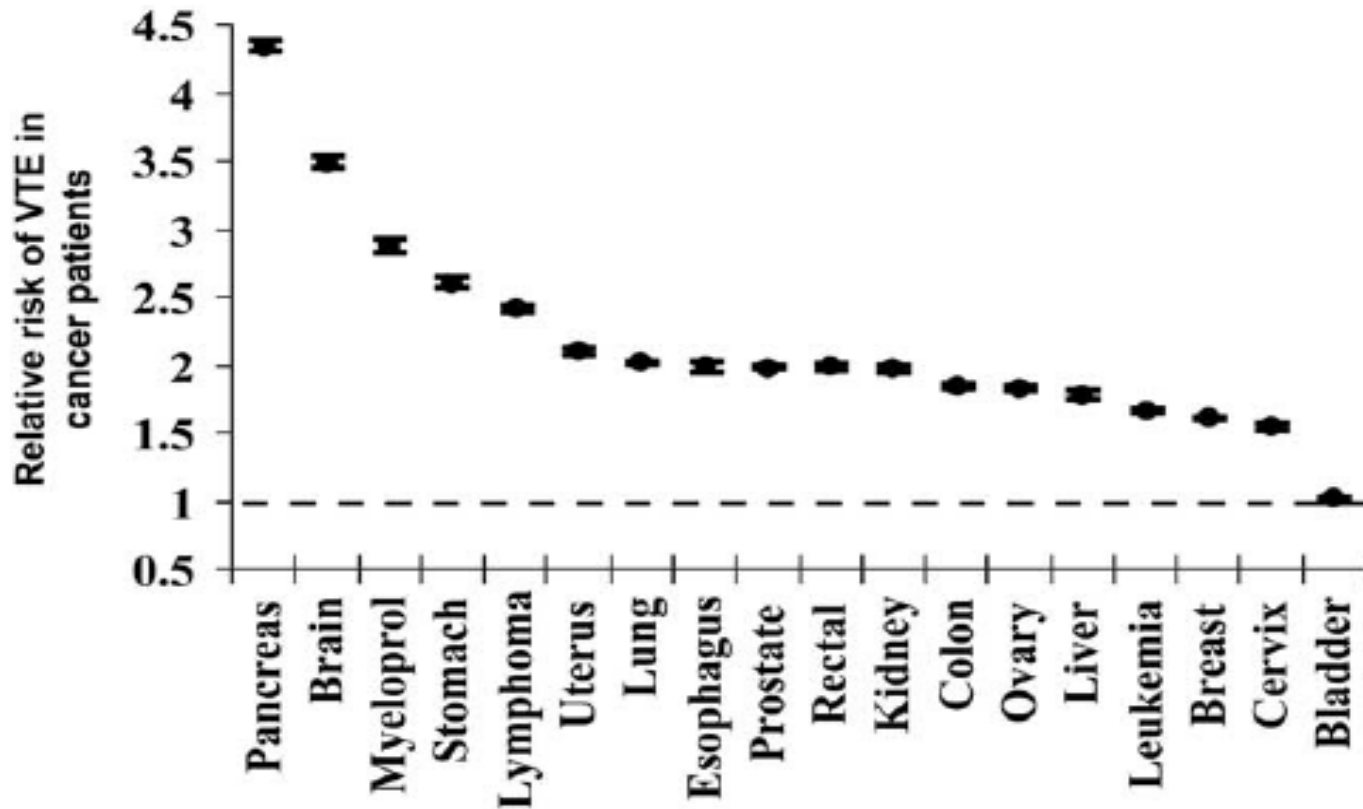
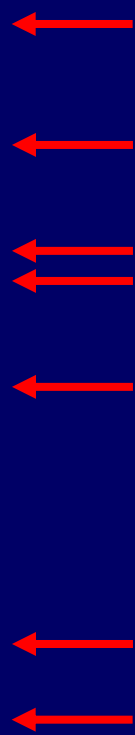


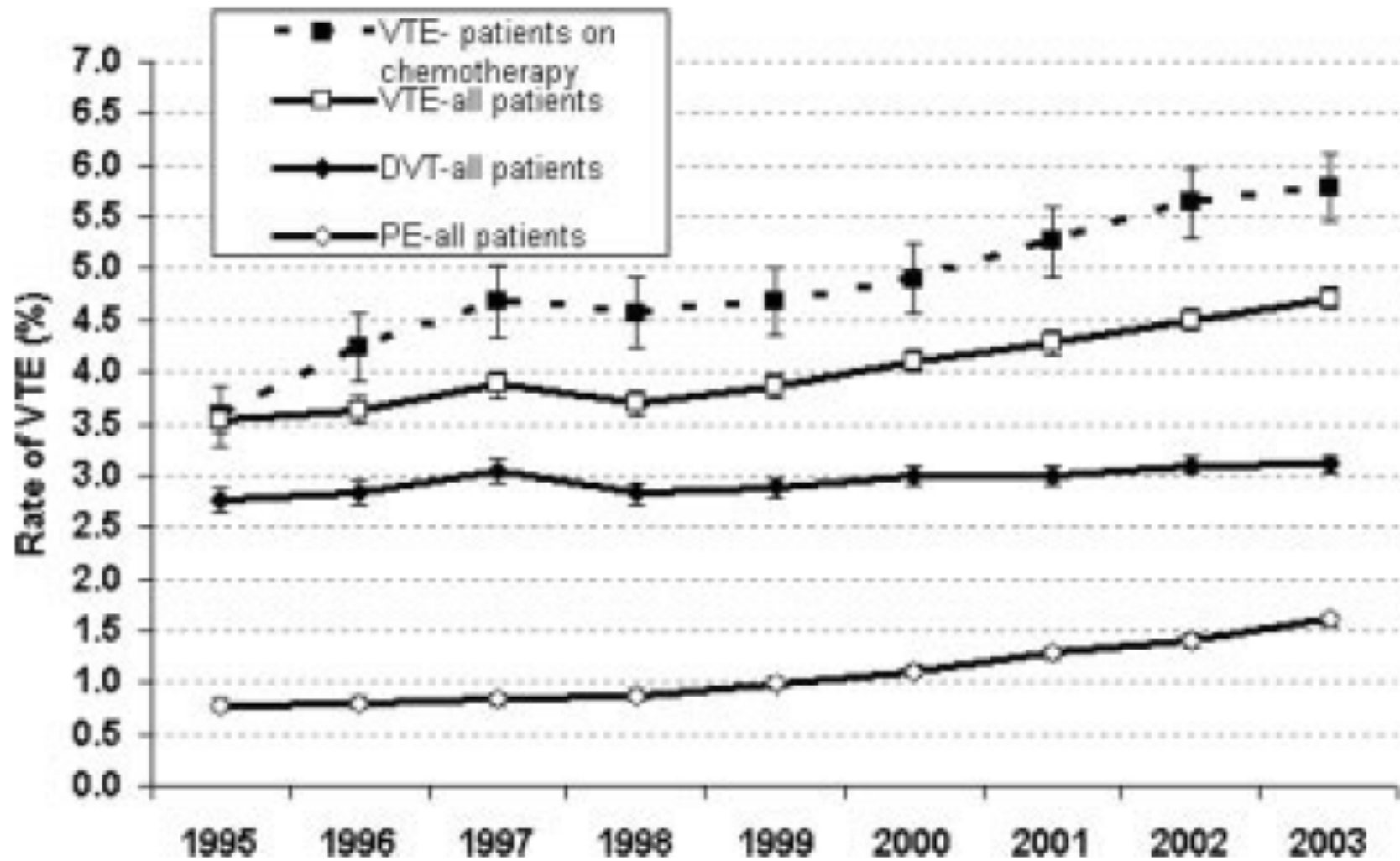
Figure 4 Relative risk of venous thromboembolism (VTE) ranged from 1.02 to 4.34.

Frequency, Risk Factors, and Trends for VTE Among Hospitalized Cancer Patients

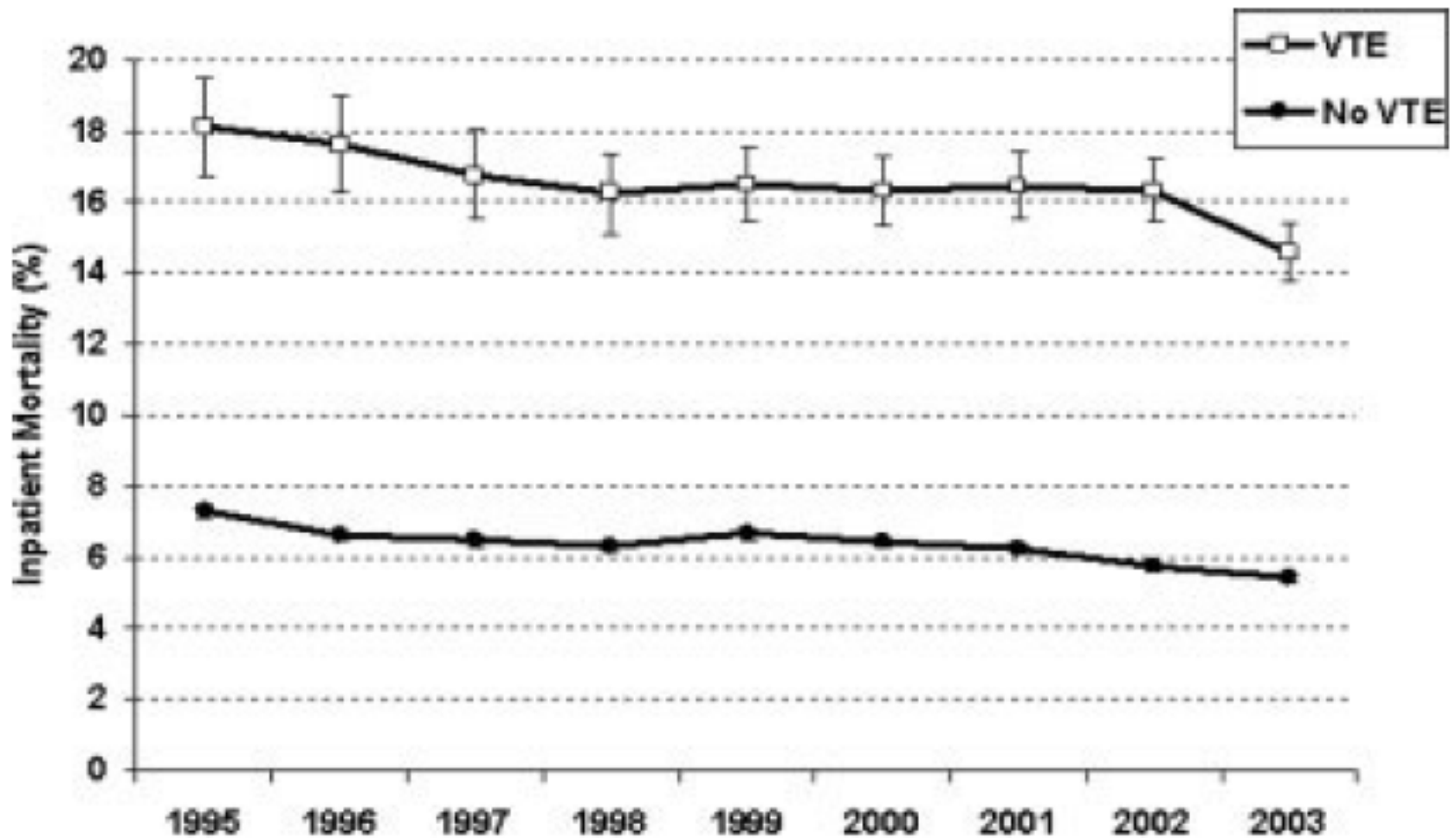
Site of Cancer and Associated Rate of Venous Thromboembolism		
Characteristic	Years 1995–2003	
	No.	% VTE
All patients	1,015,598	4.1
Sites of cancer		
<u>Lung</u>	107,587	5.1
<u>Breast</u>	70,917	2.3
Esophagus	12,274	4.3
Stomach	15,934	4.9
<u>Pancreas</u>	26,118	8.1
<u>Colon</u>	42,258	4.0
Rectum	23,287	3.5
Other abdominal	36,956	6.6
<u>Ovary</u>	23,839	5.6
Endometrium and cervix	51,445	3.5
Bladder	23,584	2.9
<u>Kidney</u>	29,651	5.6
Prostate	92,584	1.9
Testes	3687	3.3
Brain	35,297	4.7
Head and neck	50,898	1.4
Sarcoma	21,989	2.9
Non-Hodgkin lymphoma	56,964	4.8
Hodgkin disease	10,075	4.6
<u>Myeloma</u>	21,804	5.0
<u>Leukemia</u>	46,977	4.2
<u>Multiple sites</u>	18,076	5.1
Other sites	193,397	4.5



Trends for VTE Among Hospitalized Cancer Patients



VTE associated mortality Among Hospitalized Cancer Patients



Predictors of VTE

Among Hospitalized Cancer Patients

<u>Characteristic</u>	OR (95% CI)
Age 65 y	1.08 (1.05–1.1)
Female gender	1.14 (1.12–1.16)
<u>Site of cancer</u>	
Pancreas	2.46 (2.34–2.58)
Other abdominal site	1.75 (1.67–1.83)
Renal	1.71 (1.62–1.80)
Brain	1.74 (1.65–1.84)
Ovary	1.57 (1.48–1.66)
Lung	1.31 (1.27–1.35)
<u>Chemotherapy</u>	1.15 (1.12–1.18)
<u>Comorbidities</u>	
Arterial thromboembolism	1.45 (1.39–1.52)
Pulmonary disease	1.37 (1.34–1.40)
Renal disease	1.53 (1.49–1.58)
Infection	1.77 (1.73–1.81)
Anemia	1.35 (1.32–1.39)
Transfusion	1.35 (1.31–1.39)

Blood Transfusions, Thrombosis, and Mortality in Hospitalized Patients With Cancer

Khorana et al Arch Intern Med. 2008;168(21):2377

Table 2. Predictors of Venous Thromboembolism by Multivariate Logistic Regression Analysis

Characteristic	Odds Ratio (95% CI)	P Value
Age ≥65 y	1.08 (1.05-1.12)	<.001
Female sex	1.11 (1.07-1.15)	<.001
Site or type of cancer		
Pancreas	2.56 (2.36-2.77)	<.001
Brain	2.40 (2.19-2.63)	<.001
Other abdominal	2.09 (1.95-2.23)	<.001
Ovary	1.68 (1.53-1.84)	<.001
Renal	1.88 (1.73-2.04)	<.001
Lung	1.29 (1.22-1.36)	<.001
Stomach	1.36 (1.21-1.53)	<.001
Non-Hodgkin lymphoma	1.13 (1.06-1.21)	<.001
Multiple cancers	1.39 (1.24-1.55)	<.001
Race/ethnicity		
White	1 [Reference]	
Black	1.08 (1.03-1.13)	.003
Hispanic	0.99 (0.91-1.07)	.77
Asian	0.74 (0.66-0.84)	<.001
Other	1.03 (0.97-1.08)	.35
Chemotherapy	1.09 (1.05-1.15)	<.001
Venous catheters	2.00 (1.91-2.08)	<.001
Transfusions		
Red blood cell only	1.60 (1.53-1.67)	<.001
Platelet	1.20 (1.11-1.29)	<.001
Comorbidities		
Anemia	1.24 (1.19-1.29)	<.001
Infection	1.87 (1.80-1.94)	<.001
Renal disease	1.50 (1.44-1.57)	<.001
Lung disease	1.47 (1.42-1.53)	<.001

**RBC
PLT**

**1.60 (1.53-1.67)
1.20 (1.11-1.29)**

Incidence of VTE in ambulatory cancer patients

**Retrospective study in 206 cancer patients receiving
chemotherapy**

VTE incidence*: 7.3% (15/206)

Annual incidence of VTE: 10.9 %

*** (during treatment or within 3 months)**

Incidence of DVT in patients treated with thalidomide

	N	DVT	Disease
Zangari, 2001	50	14 (28%)	Multiple myeloma
Osman, 2001	15	4 (27 %)	Multiple myeloma
Urbauer, 2002	14	3 (21%)	Multiple myeloma
Urbauer, 2002	10	2 (20%)	Lymphoma
Valprè, 2002	19	5 (26%)	Multiple myeloma
Zangari, 2003	535	82 (15%)	Multiple myeloma

Thalidomide and thrombosis

A meta-analysis

	VTE events		Bi-variate p-value	Multivariate p-value (OR, 95% CI)
	Yes N (%)	No N (%)		
Thalidomide				
Yes	331 (12.5)	2296 (87.5)	<0.01	<0.01 (2.6, 1.8–3.6)
No*	45 (6.5)	650 (93.5)	-	
Dexamethasone				
Yes	349 (12.8)	2373 (87.2)	<0.01	<0.01 (2.8, 1.8–4.3)
No*	27 (4.5)	573 (95.5)	-	
Other chemotherapy				
Yes	291 (12.6)	2015 (87.4)	<0.01	0.01 (1.5, 1.1–2.0)
No*	85 (8.4)	931 (91.6%)		

2.6 (1.8-3.6)

2.8 (1.8-4.3)

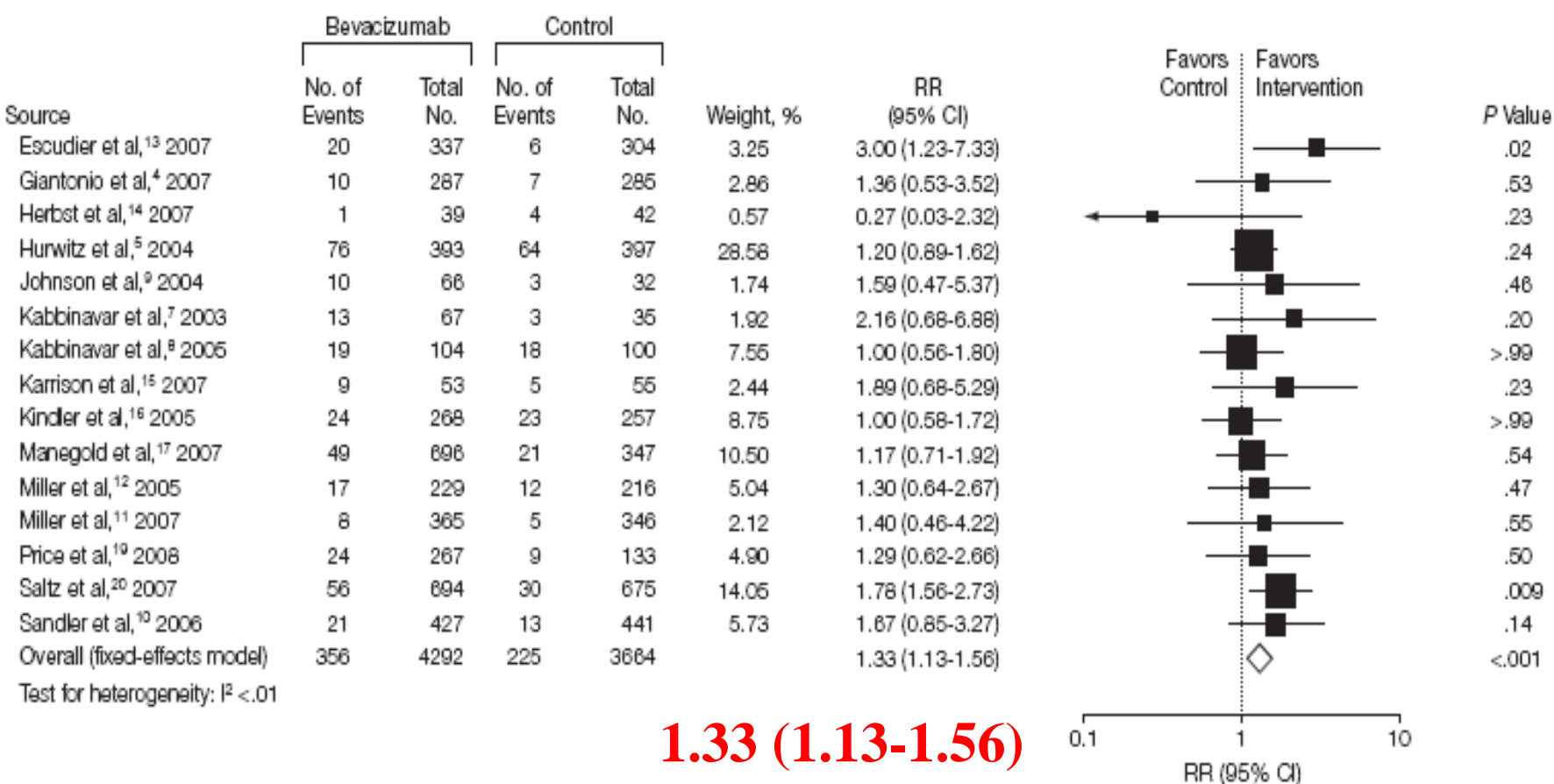
Thromboembolic Events With Lenalidomide-based Therapy for Multiple Myeloma

Patiyil Menon et al.
Cancer 2008;112:1522

Study	Regimen	Disease status	No. of patients	Rate of deep vein thrombosis	Thromboprophylaxis
Dimopoulos, 2005 ¹⁸	Lenalidomide 25 mg Days 1-21 every 28 d plus dexamethasone 40 mg Days 1-4, 9-12, 17-20 every 28 d	Relapsed, refractory	176	8.5%	None
Weber, 2006 ²⁷	Lenalidomide 25 mg Days 1-21 every 28 d plus dexamethasone 40 mg Days 1-4, 9-12, 17-20 every 28 d	Relapsed, refractory	177	15%	None
Zonder, 2005 ²⁵	Lenalidomide 25 mg Days 1-28 every 35 d plus dexamethasone 40 mg Days 1-4, 9-12, 17-20 every 35 d	Newly diagnosed	38	75%; reduced to 19% after institution of aspirin prophylaxis	ASA in the second phase
Richardson, 2006 ²⁸	Lenalidomide 30 mg daily (or 15 mg twice a d) administered on Days 1-21 every 28 dd with or without dexamethasone Days 1-4, 15-18 every 28 d	Relapsed, refractory	102	3% (rate is 4.4% among the 68 patients who received lenalidomide plus dexamethasone)	None
Rajkumar, 2007 ²⁶	Lenalidomide 25 mg Days 1-21 every 28 d plus dexamethasone 40 mg Days 1-4, 9-12, 17-20 every 28 d	Newly diagnosed	223	22.1%	ASA (randomized between coumadin and ASA in the expansion phase)
Rajkumar, 2007 ²⁶	Lenalidomide 25 mg Days 1-21 every 28 d plus dexamethasone 40 mg Days 1, 8, 15, 22 every 28 d	Relapsed, refractory	222	6.1%	ASA

DVT incidence 3-22%

Figure 2. Relative Risk (RR) of Venous Thromboembolism Associated With Bevacizumab vs Control

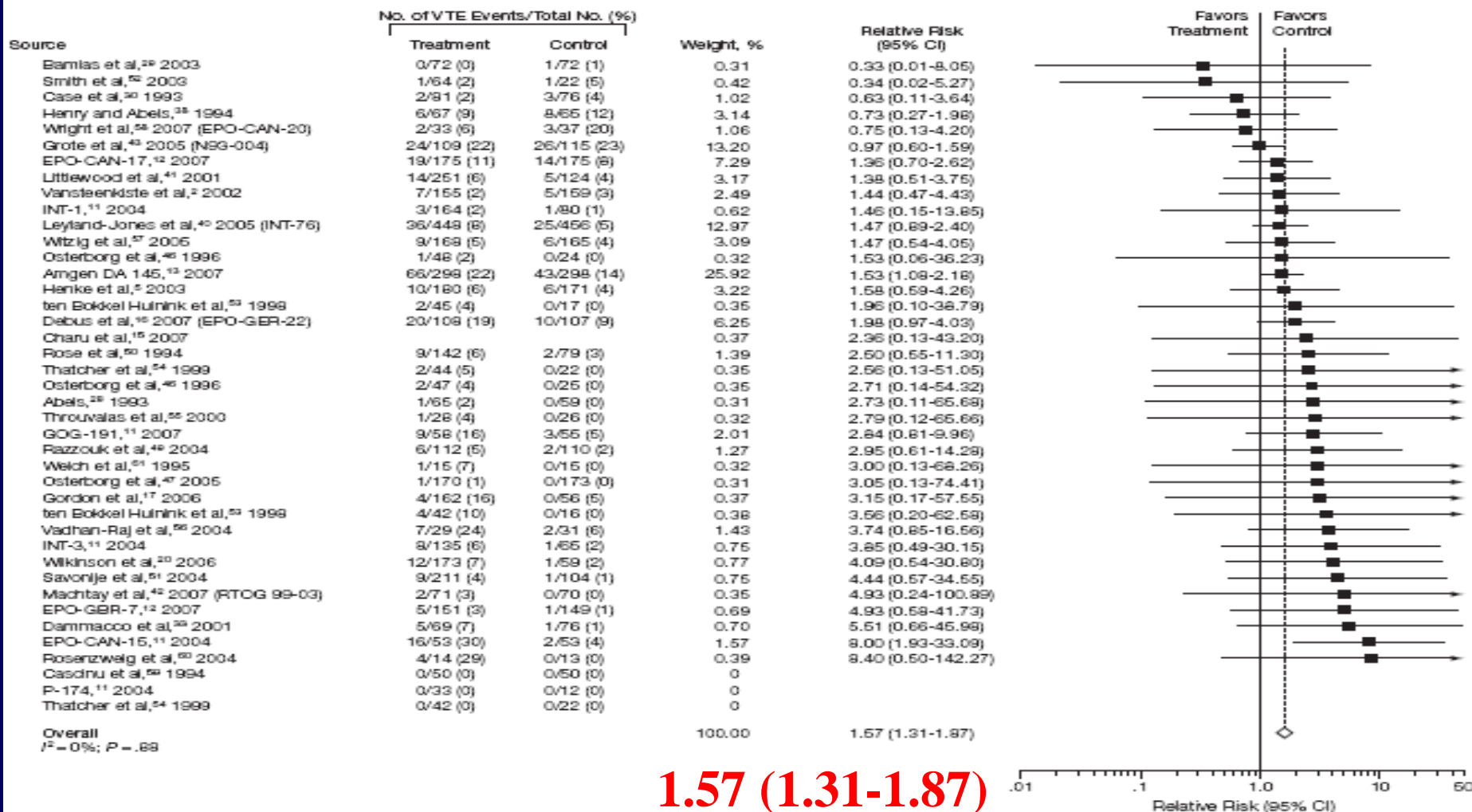


Venous Thromboembolism and Mortality Associated With Recombinant Erythropoietin and Darbepoetin Administration for the Treatment of Cancer-Associated Anemia

Charles L. Bennett; Samuel M. Silver; Benjamin Djulbegovic; et al.

JAMA. 2008;299(8):914-924 (doi:10.1001/jama.299.8.914)

Figure 3. Meta-analysis of VTE Rates in Phase 3 Trials of ESAs vs Placebo or Control



1.57 (1.31-1.87)

Radiotherapy and VTE risk

Patients with colorectal cancer

	RT	No RT	p	RR
Total VTE	7.5%	3.6%	0.001	2

Pathogenesis of venous thromboembolism

On the whole, VTE is probably best understood as a “multi-causal” disease in which more than one genetic or environmental conditions coincide to produce clinically apparent thrombosis

Venous thrombosis: a multicausal disease

Rosendaal FR

Lancet. 1999;353:1167-1173

Development and validation of a predictive model for chemotherapy-associated thrombosis

Alok A. Khorana, Nicole M. Kuderer, Eva Culakova, Gary H. Lyman and Charles W. Francis

Table 3. Predictive model for chemotherapy-associated VTE

Patient characteristic	Risk score
Site of cancer	
Very high risk (stomach, pancreas)	2
High risk (lung, lymphoma, gynecologic, bladder, testicular)	1
Prechemotherapy platelet count $350 \times 10^9/L$ or more	1
Hemoglobin level less than 100 g/L or use of red cell growth factors	1
Prechemotherapy leukocyte count more than $11 \times 10^9/L$	1
BMI 35 kg/m^2 or more	1

blood

2008 111: 4902-4907
Prepublished online Jan 23, 2008;
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