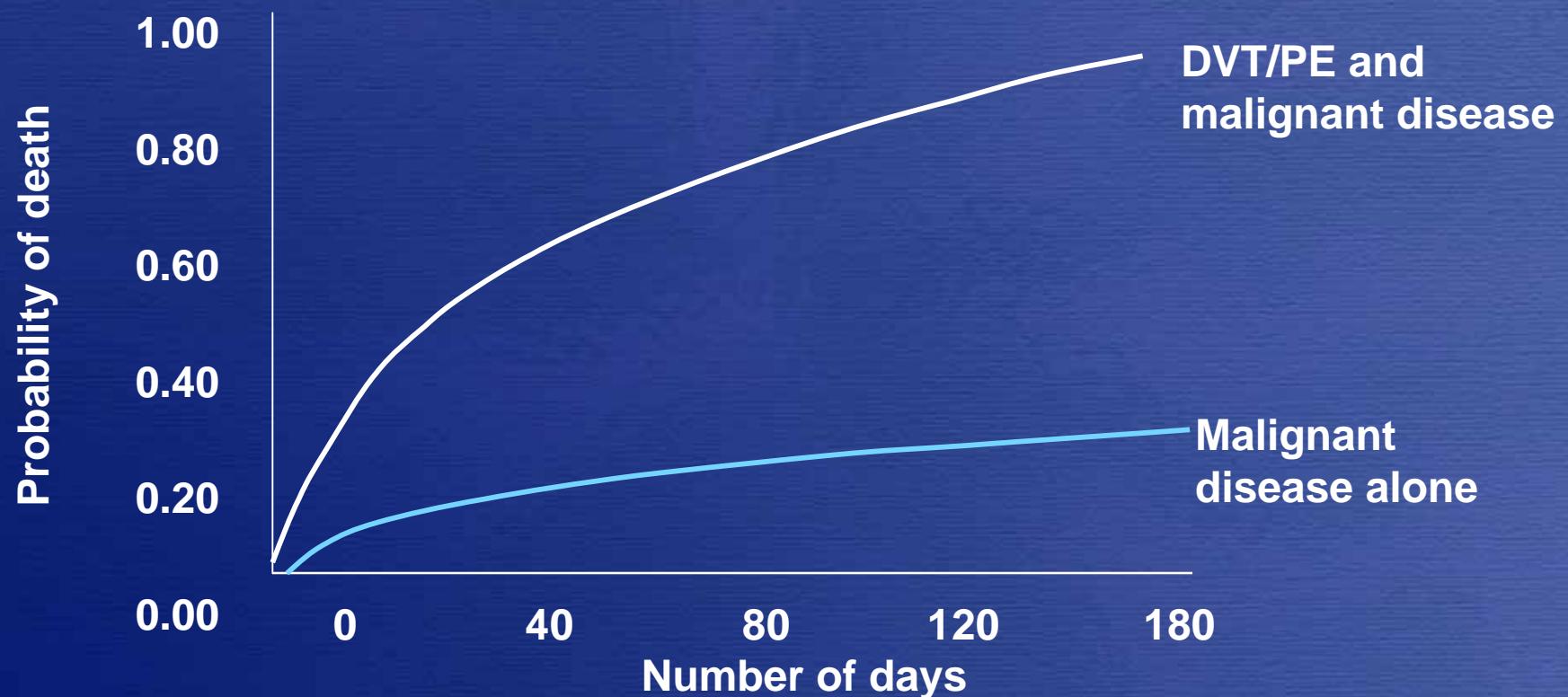


# **High risk populations: Cancer**

**Professor A K Kakkar**

# Concurrent VTE and cancer increases the risk of death

Probability of death within 183 days of initial hospital admission



Levitin N, et al. "Rates of thromboembolic disease among patients with malignancy versus those without malignancy: Risk analysis using Medicare claims data." Medicine 1999; 78:285-291

# Activation of coagulation in cancer patients

|                    | Control<br>(n = 72) | Cancer<br>(n = 106) | p      |
|--------------------|---------------------|---------------------|--------|
| TF, pg/mL          | 349                 | 582                 | 0.0006 |
| Factor VIIa, ng/mL | 69                  | 100                 | 0.0002 |
| TAT, g/L           | 2.0                 | 8.0                 | 0.0001 |
| PF1+2, ng/mL       | 1.0                 | 3.0                 | 0.0001 |
| Factor XIIa, ng/mL | 2.0                 | 3.0                 | 0.02   |

PF = prothrombin fragment; TAT = thrombin-antithrombin complex; TF = tissue factor.

Kakkar A, et al. Lancet. 1995;346:1004-5.

# Cancer and PE

|                     | At risk | Number         |                    | Overall incidence, % | 95% CI | OR        |
|---------------------|---------|----------------|--------------------|----------------------|--------|-----------|
|                     |         | In-Hospital PE | After-discharge PE |                      |        |           |
| Surgical Cancer     | 1,796   | 40             | 2                  | 42                   | 2.34   | 1.69–3.15 |
| No cancer           | 17,365  | 40             | 22                 | 62                   | 0.36   | 0.27–0.46 |
| Non surgical Cancer | 815     | 5              | 1                  | 6                    | 0.73   | 0.27–1.60 |
| No cancer           | 8,977   | 5              | 4                  | 9                    | 0.10   | 0.50–0.19 |

Huber O, et al. Arch Surg. 1992;127:310-3.

# ACCP Consensus conference on antithrombotic therapy

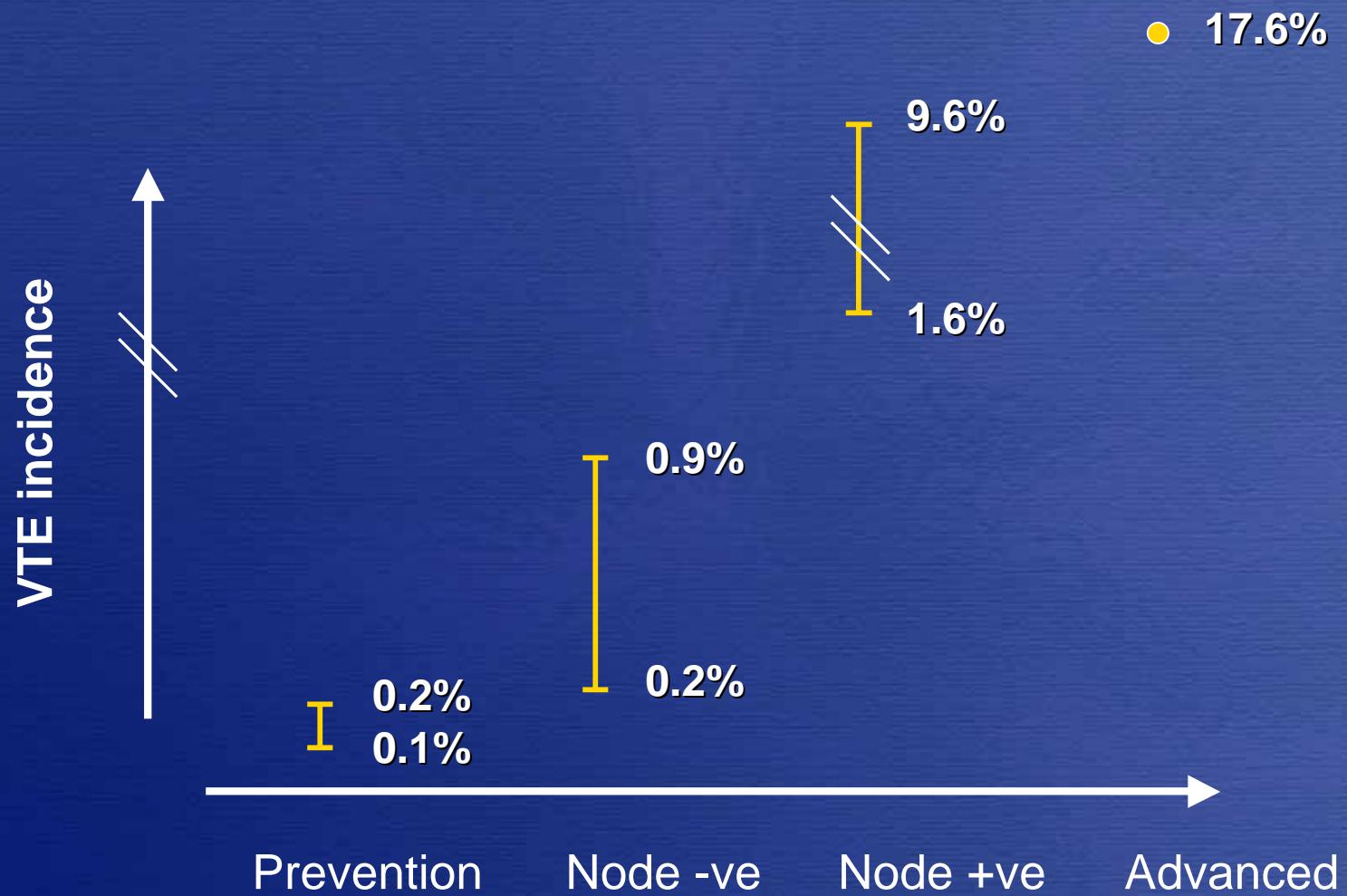
## Major surgery in cancer patients

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

Geerts et al  
Chest 2004

ACCP, American College of Chest Physicians; PE, pulmonary embolism.

# Incidence of VTE in malignancy: non-surgical breast cancer

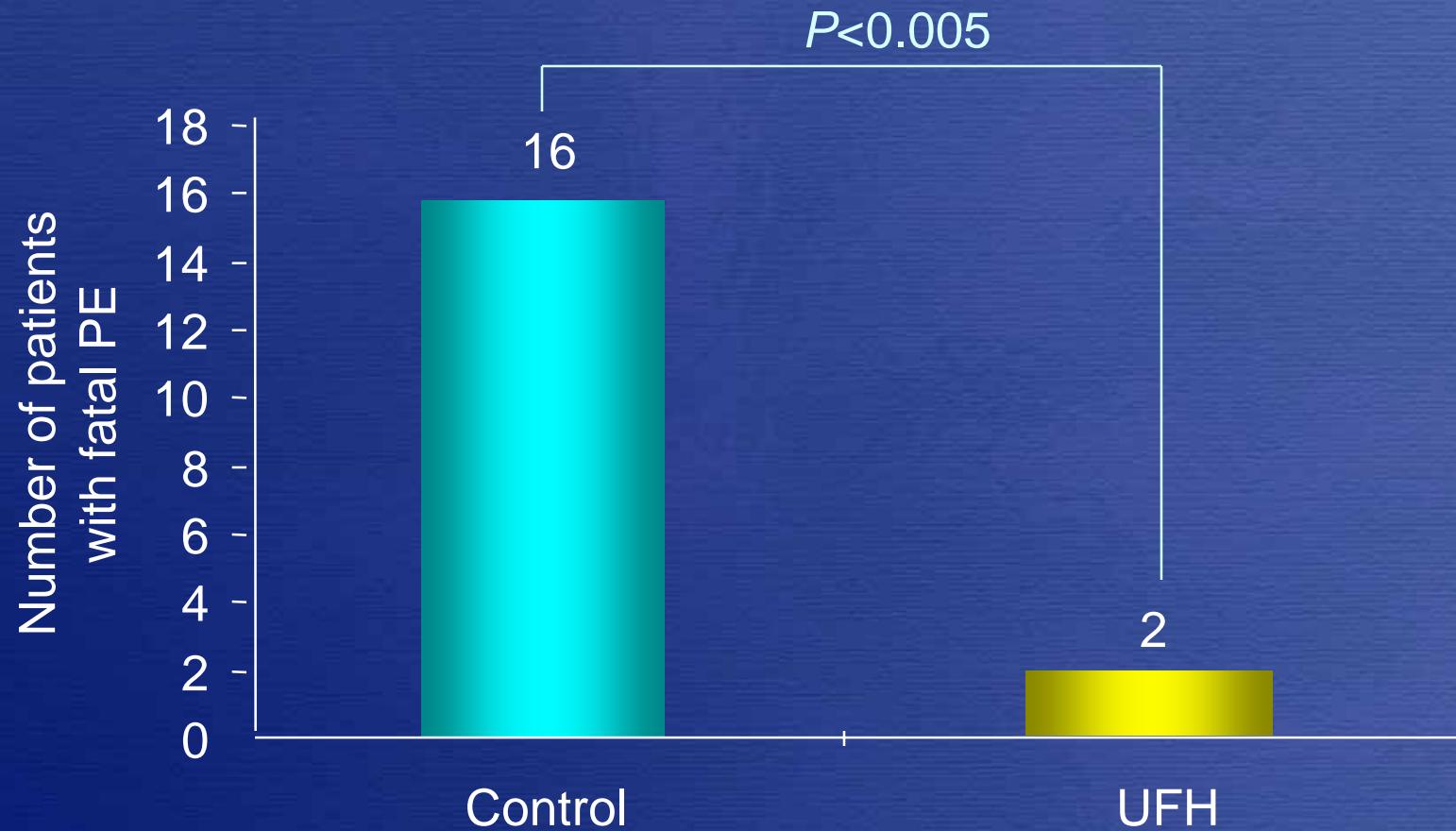


# Incidence of VTE in malignancy: non-surgical other cancers

|                    | Incidence of VTE % |
|--------------------|--------------------|
| Ovarian            | 10                 |
| Glioma             | 7 - 24             |
| Lymphoma           | 4 - 6              |
| Germ cell          | 8                  |
| Anti-VEGF in colon | 19                 |

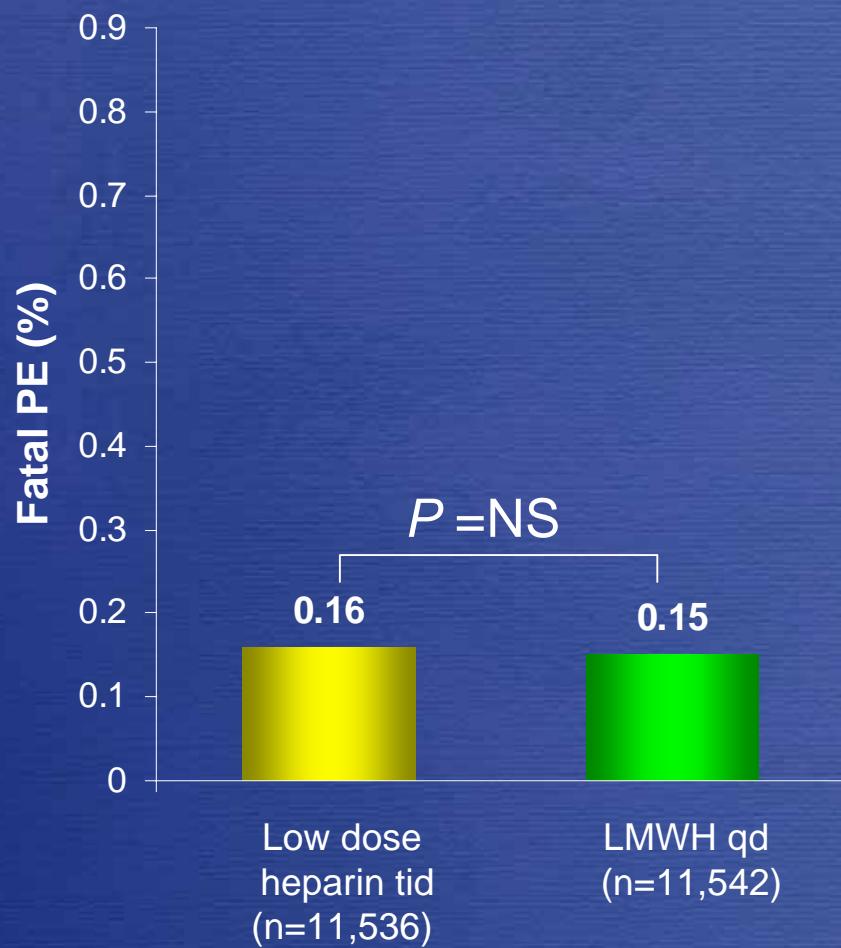
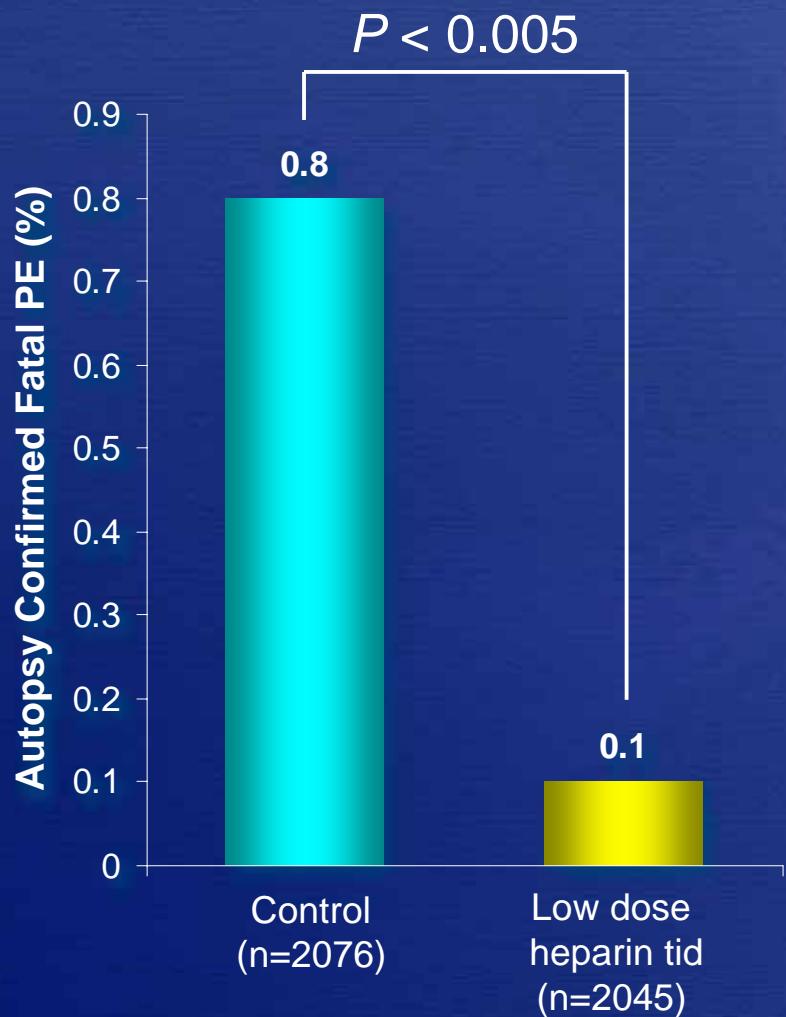
LIMITED DATA

# Prophylaxis against Fatal Post-operative PE with Low-dose UFH



Kakkar vv et al Lancet 1975;2:45–51

# Prevention of Fatal Pulmonary Embolism



Kakkar VV et al. Lancet. 1975;2:45-51; Haas S, et al. Thromb Haem. 2005.

# Bleeding driven by pathology

|                                  | Cancer surgery<br>(n = 6,124) | Non-cancer surgery<br>(n = 16,954) | p        |
|----------------------------------|-------------------------------|------------------------------------|----------|
| Re-operation because of bleeding |                               |                                    |          |
| Patients, n (%)                  | 68 (1.1%)                     | 102 (0.6%)                         | < 0.001* |
| Transfusion of whole blood       |                               |                                    |          |
| Patients, n (%)                  | 483 (7.9%)                    | 890 (5.2%)                         | 0.001*   |
| Mean volume, mL (SD)             | 1,028 (862)                   | 752 (507)                          | 0.001†   |
| Median volume, mL (range)        | 750 (120–8,000)               | 750 (600–4,000)                    |          |
| Bleeding complications           |                               |                                    |          |
| Wound haematoma                  | 198                           | 293                                | 0.001*   |
| Post-operative wound bleeding    | 33                            | 36                                 |          |
| Gastric bleeding                 | 7                             | 2                                  |          |
| Intestinal bleeding              | 5                             | 2                                  |          |

\*Calculated using Fisher's Test. †Calculated using the Wilcoxon Test.

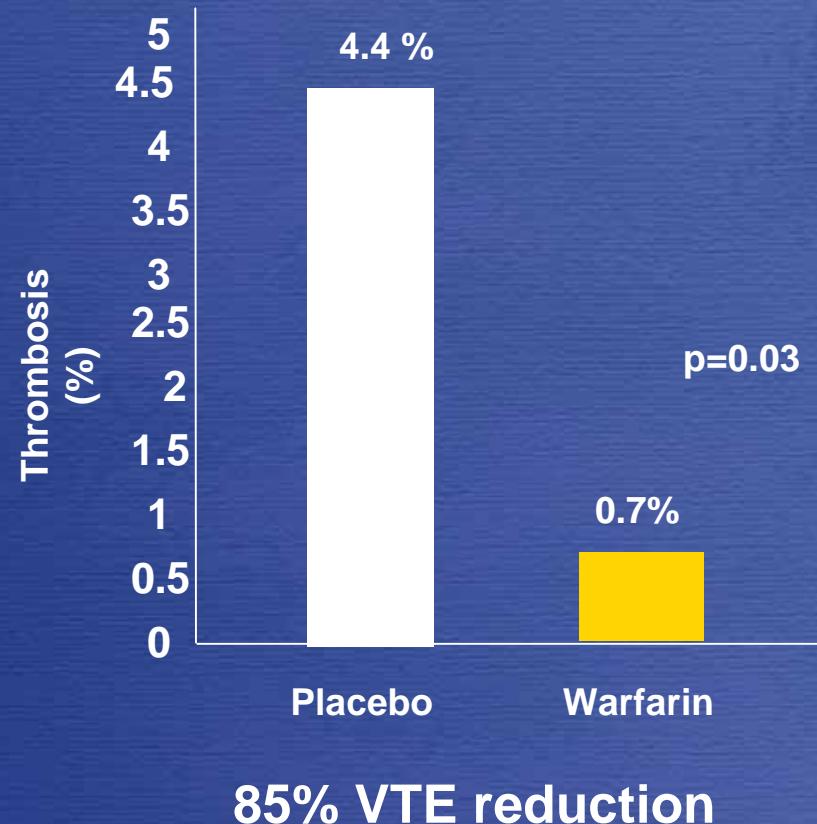
Kakkar AK, et al. Thromb Haemost. 2005;94:867-71.

## PE and Death: Cancer vs. No Cancer

| All patients (low-dose UFH or LMWH) | Cancer (n=6124) | No cancer (n=16,954) | P value |
|-------------------------------------|-----------------|----------------------|---------|
| Death (%)                           | 192 (3.1)       | 120 (0.7)            | 0.0001  |
| Fatal PE (%)                        | 20 (0.33)       | 15 (0.09)            | 0.0001  |
| Non-fatal PE (%)                    | 5 (0.08)        | 4 (0.02)             |         |

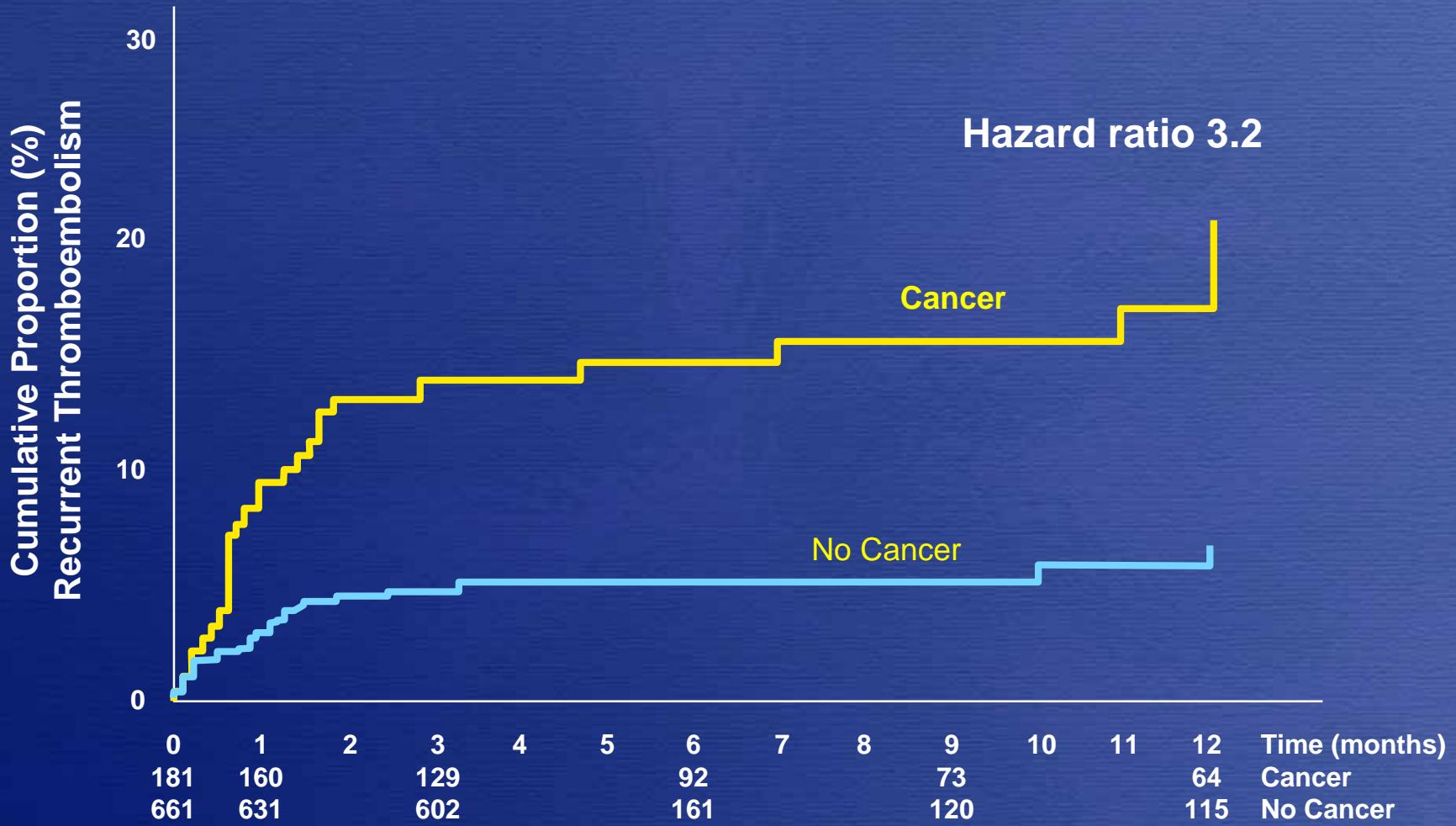
# Prophylaxis: ambulant patient

- 311 women with advanced breast cancer
- Low-dose warfarin INR 1.3–1.9



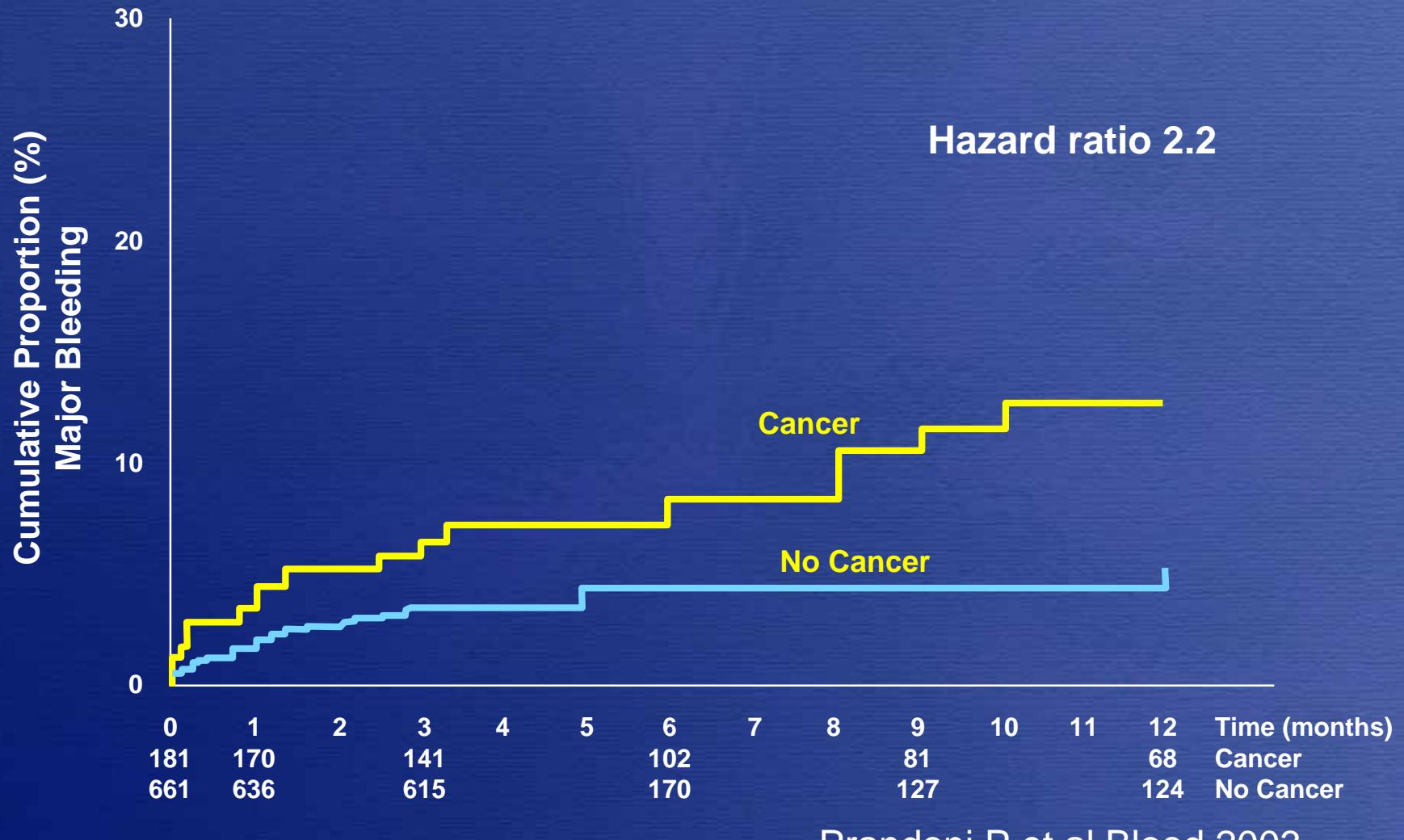
Levine M et al. *Lancet* 1994;886:886–9

# Cumulative Incidence of Recurrent VTE During Anticoagulant Therapy



Prandoni P et al Blood 2003

# Cumulative Incidence of Clinically Important Bleeding During Anticoagulant Therapy



# LMWH and survival

|                                   | Therapy    | Median survival, months |                           | p     |
|-----------------------------------|------------|-------------------------|---------------------------|-------|
|                                   |            | Overall population      | Good prognosis population |       |
| FAMOUS <sup>1</sup><br>(2002)     | Daltaparin | 10.80                   | 43.5                      | 0.03  |
|                                   | Placebo    | 9.14                    | 24.3                      |       |
| SCLC study <sup>2</sup><br>(2003) | Daltaparin | 13.0                    | 16.0                      | 0.007 |
|                                   | Placebo    | 8.0                     | 10.0                      |       |
| MALT <sup>3</sup><br>(2003)       | Daltaparin | 8.0                     | 15.4                      | 0.01  |
|                                   | Placebo    | 6.6 (HR 1.0)            | 9.4 (HR 0.64)             |       |
| 1-year survival, %                |            |                         |                           |       |
| CLOT <sup>4</sup><br>(2003)       | Dalteparin | 62                      | 80                        | 0.03  |
|                                   | OAC        | 61 (HR 1.0)             | 64 (HR 0.5)               |       |

HR = hazard ratio; OAC = oral anticoagulant.

<sup>1</sup>Kakkar AK, et al. J Clin Oncol. 2004;22:1944-8;

<sup>2</sup>Altinbas M, et al. J Thromb Haemost. 2004;2:1266-71;

<sup>3</sup>Klerk CP, et al. J Clin Oncol. 2005;23:2130-5;

<sup>4</sup>Lee AY, et al. N Engl J Med. 2003;349:146-53.