



Cancer Associated Venous Thromboembolism: Epidemiology and Impact of VTE on Survival

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Background

Our research group's first study of the epidemiology of cancer-associated thrombosis (CAT) analyzed data gathered between 1993-1995.

(Chew et al, 2006)

We now present a larger, more contemporary analysis from 2005-2014.

Enhancements include:

- ❖ A larger sample size.
- ❖ The availability of ICD-9-CM codes for *proximal* and *distal* DVT.
- ❖ Results that reflect the improved detection of CAT (US & CTangio)
- ❖ Adjustment of models to account for *the competing risk of death*.
- ❖ Results that reflect advances in the treatment of many cancers.
- ❖ Addition of brain cancer and myeloma to prior analysis.

Our Aims

- To characterize the epidemiology of CAT in a more contemporary era.
- To better characterize racial/ethnic differences in the incidence of CAT.
- To determine if the development of calf DVT alone is associated with a reduced adjusted-risk of survival.

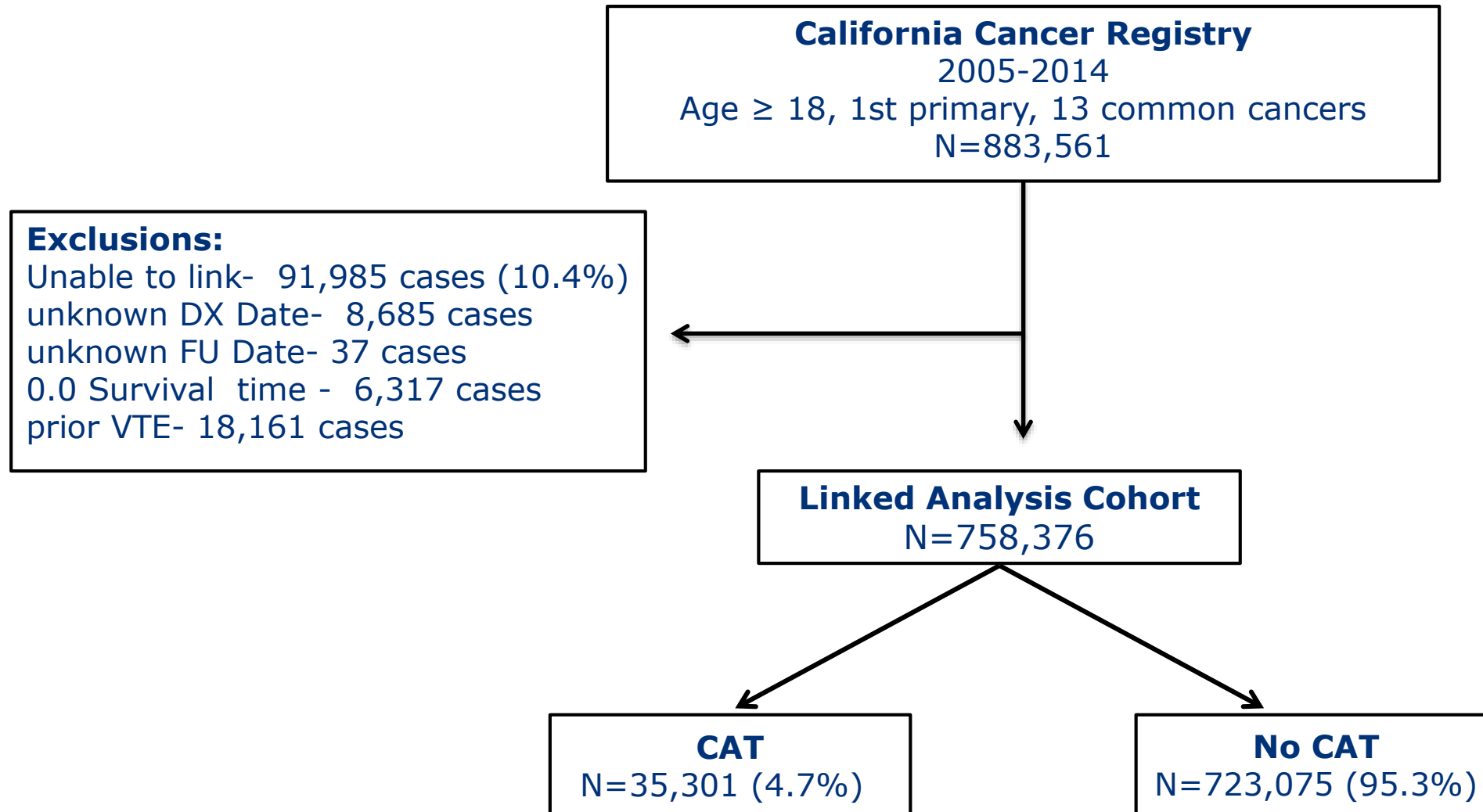
Methods

- Cancer cases were identified using the California Cancer Registry.
 - First primary was Dx'd between 2005-2014, with no cancer back to 1988.
 - Age ≥ 18 on day of cancer diagnosis.
- Cancers were *linked* to State of California Hospital Discharge Data, the Emergency Department Data, and the National Master Death Registry.
 - This allows follow-up of sequential hospital, ED encounters and death over time.
- Complete follow-up was available through December 2014.
- VTE was defined using specific ICD-9-CM codes (including prox/distal)
- Covariates included age, race, sex, cancer diagnosis date, cancer type, cancer stage, initial course of Tx, neighborhood SES, and initial health insurance

Methods- 13 Common Cancers in this Study

- Breast
- Prostate
- Lung and Bronchus
- Colorectal
- Lymphoma
- Urinary Bladder
- Corpus Uteri and Uterus, NOS
- Kidney and Renal Pelvis
- Pancreas
- Stomach
- Ovary
- Brain
- Myeloma

Methods- Cohort Diagram



Methods- Analysis Plan

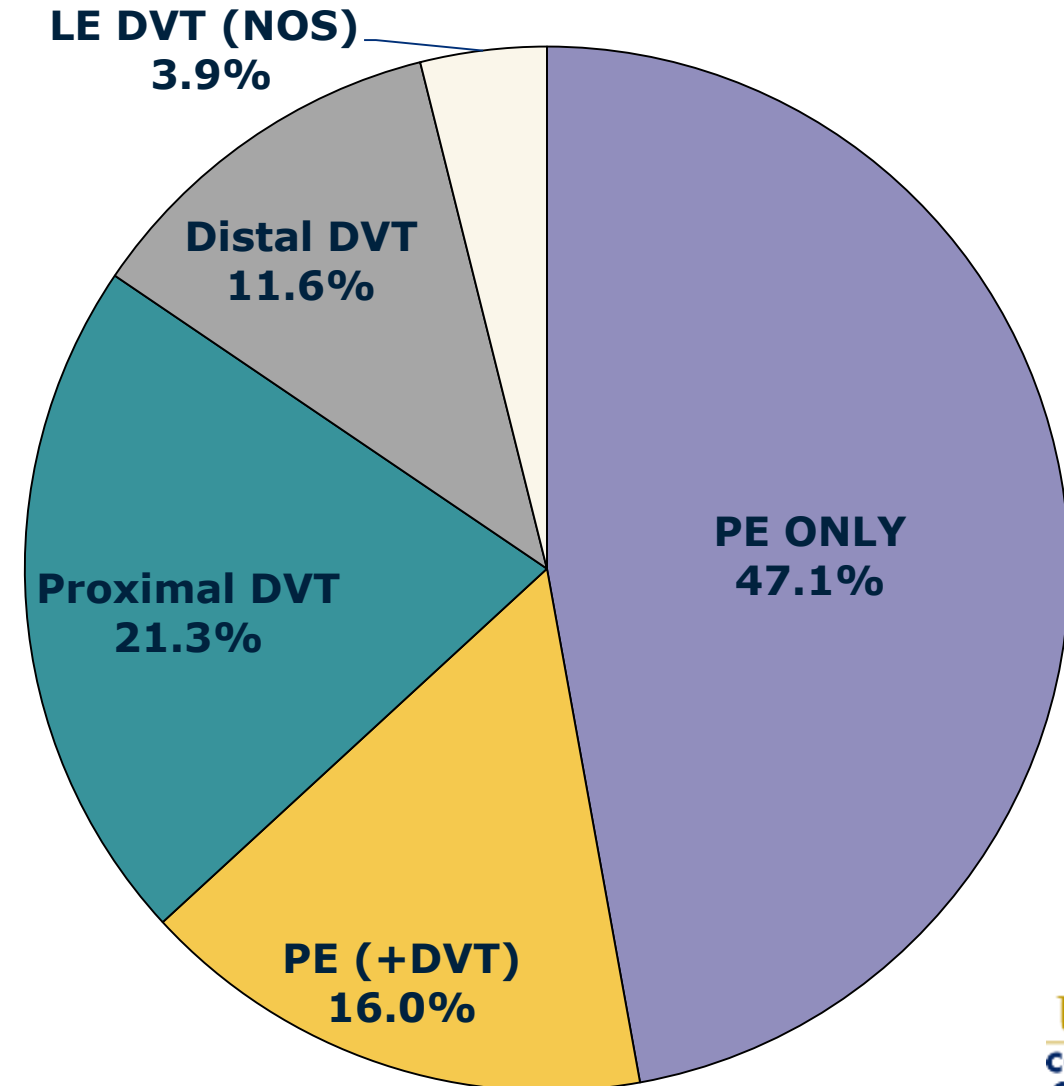
- We determined the Cumulative Incidence Function of the 2 year incidence of CAT, adjusted for the competing risk of death.
- We modeled risk factors associated with a Dx of CAT < 2yrs and used Proportional Hazard Regression, with stratification and adjustment for specific risk factors, including the competing risk of death.
- We also used Proportional Hazard Regression to estimate risk factors associated with mortality.
 - In these models, first CAT (or CAT location) was entered as a time-dependent covariate.

Results – Frequency of CAT by Cancer Type

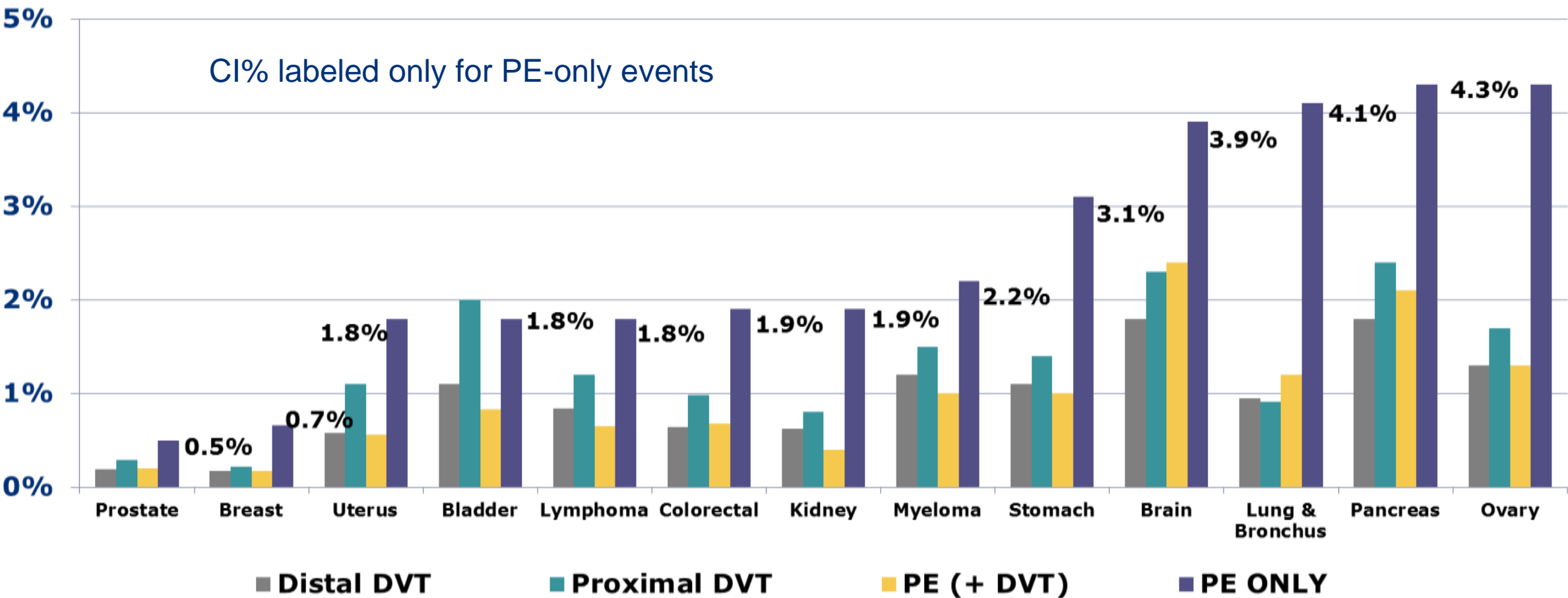
Cancer Site	Cancer Cases		CAT Cases	
	N	%	N	%
All	758,376	100.0%	35,301	4.7%
Breast	170,901	22.5%	3,608	2.1%
Prostate	145,375	19.2%	3,321	2.3%
Lung and Bronchus	103,815	13.7%	7,941	7.6%
Colorectal	97,989	12.9%	4,922	5.0%
Lymphoma	43,327	5.7%	2,289	5.3%
Urinary Bladder	39,452	5.2%	1,761	4.5%
Corpus Uteri and Uterus, NOS	35,575	4.7%	1,789	5.0%
Kidney and Renal Pelvis	32,274	4.3%	1,445	4.5%
Pancreas	27,110	3.6%	2,851	10.5%
Stomach	18,856	2.5%	1,293	6.9%
Ovary	16,945	2.2%	1,736	10.2%
Brain	13,324	1.8%	1,402	10.5%
Myeloma	13,433	1.8%	943	7.0%

Results – Proportion of CAT Events, by Location of Clot

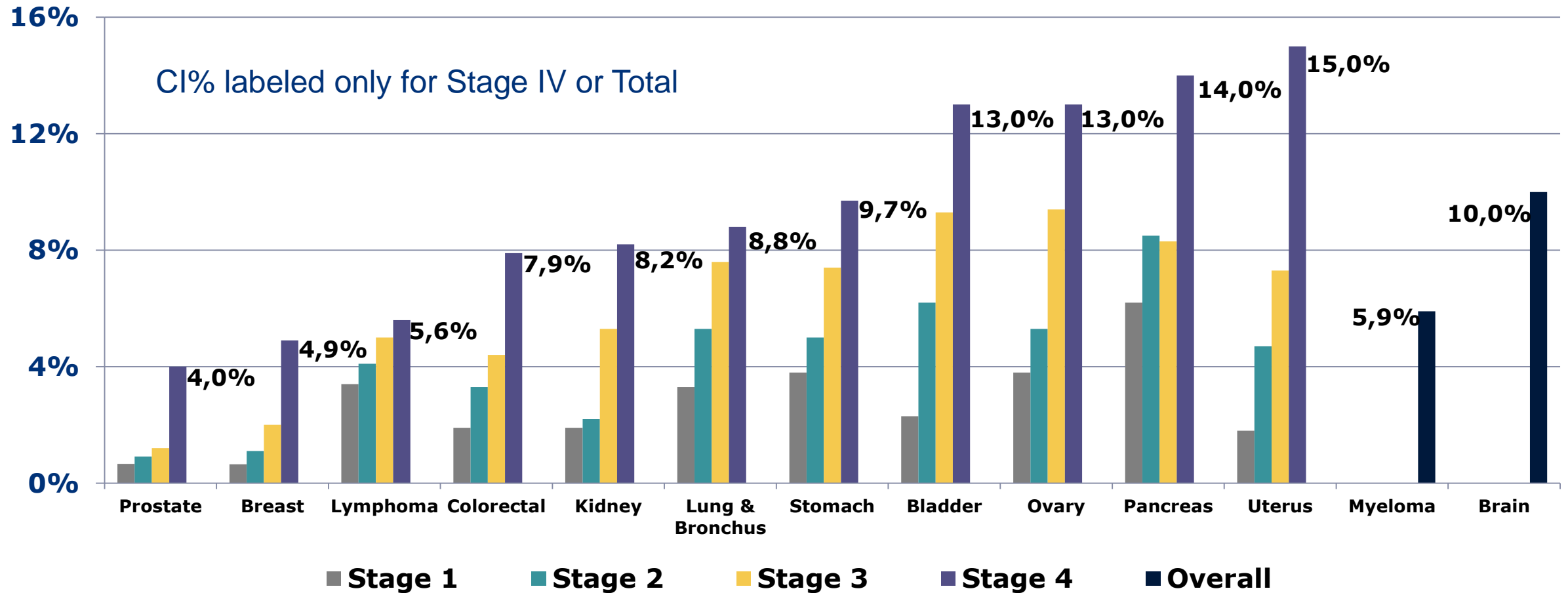
- 758,376 Cancer Cases
- 35,301 (4.7%) were diagnosed with CAT during the follow up period



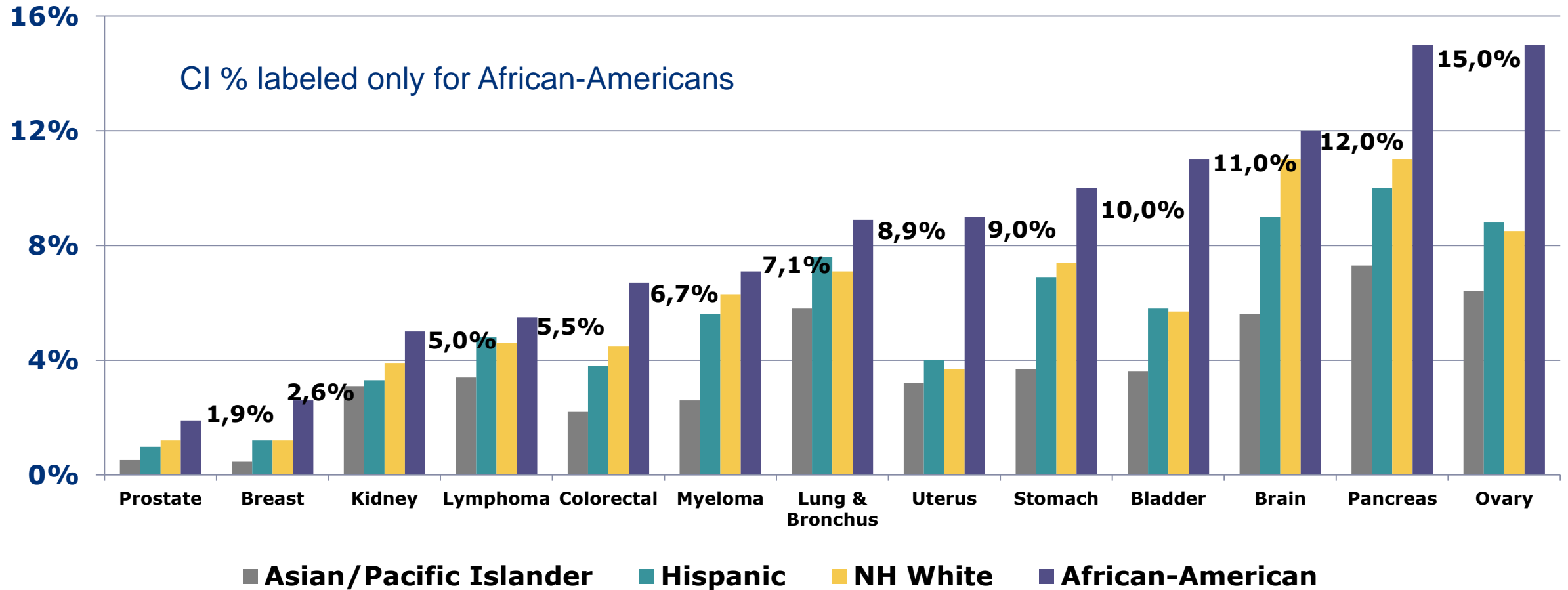
*Results – 2 year Cumulative Incidence of CAT < 2 yrs.
by different Cancer Types, by CAT Location.*



Results – 2 year Cumulative Incidence of CAT for Different Cancer Types, by Cancer Stage



Results – 2 year Cumulative Incidence of CAT by Different Cancer Types, by different Race/Ethnicity.



Results – Effect of Sex, Race & Age on Risk of CAT< 2 yr

Stratified by Initial Tx & Stage, Adjusted for Competing Risk of Death

Variables	HR	95% CI	P-Value
Gender			
Female	0.99	(0.96, 1.02)	0.4758
Male	Reference	-	-
Race/Ethnicity			
NH White	Reference	-	-
African American	1.43	(1.37, 1.49)	<.0001
Hispanic	0.93	(0.89, 0.96)	<.0001
Asian/PI	0.62	(0.59, 0.65)	<.0001
Age at Diagnosis			
< 50	Reference	-	-
50-59	1.13	(1.08, 1.19)	<.0001
60-69	1.20	(1.15, 1.26)	<.0001
70-79	1.26	(1.20, 1.33)	<.0001
≥ 80	1.12	(1.05, 1.19)	0.0002

Model was stratified by surgery, radiation, chemotherapy, and stage at diagnosis, adjusted for the competing risk of death.

Model adjusted for health insurance, neighborhood socioeconomic status, and cancer type

Results – Effect of Cancer Type on Risk of CAT< 2 yrs.

Stratified by Initial Tx & Stage, Adjusted for Competing Risk of Death

Variables	HR	95% CI	P-Value
Cancer Site			
Breast	Reference	-	-
Prostate	0.91	(0.83, 0.99)	0.0345
Lymphoma	1.83	(1.69, 1.98)	<.0001
Colorectal	2.19	(2.05, 2.34)	<.0001
Kidney and Renal Pelvis	2.53	(2.32, 2.76)	<.0001
Lung and Bronchus	2.74	(2.55, 2.93)	<.0001
Myeloma	2.77	(2.43, 3.15)	<.0001
Stomach	3.22	(2.96, 3.51)	<.0001
Corpus Uteri and Uterus, NOS	3.60	(3.33, 3.89)	<.0001
Urinary Bladder	3.86	(3.54, 4.21)	<.0001
Ovary	4.10	(3.78, 4.45)	<.0001
Pancreas	4.63	(4.30, 4.99)	<.0001
Brain	4.98	(4.47, 5.54)	<.0001

Model was stratified by initial Tx (surgery, rad, chemo), and stage at diagnosis, adjusted for the competing risk of death.

Model adjusted for health insurance and neighborhood socioeconomic status, demographics

Results – Effect of CAT Location on the Risk of Death, Adjusted for age, race, sex, stage, initial Tx, insurance, SES, marital status

Cancer Site	PE Only		PE + DVT		Proximal DVT		Distal DVT	
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
Prostate	4.95	(4.56, 5.36)	4.06	(3.56, 4.63)	4.50	(4.08, 4.96)	4.63	(4.11, 5.22)
Corpus Uteri/Uterus	4.55	(4.15, 4.99)	3.60	(3.06, 4.23)	5.68	(5.08, 6.35)	4.54	(3.94, 5.24)
Lymphoma	3.45	(3.17, 3.76)	3.29	(2.86, 3.78)	3.82	(3.47, 4.21)	3.63	(3.22, 4.10)
Breast	4.70	(4.40, 5.01)	4.10	(3.61, 4.66)	4.73	(4.28, 5.23)	3.57	(3.19, 4.00)
Ovary	2.76	(2.54, 3.00)	2.43	(2.10, 2.82)	3.29	(2.92, 3.70)	3.16	(2.76, 3.63)
Urinary Bladder	2.64	(2.34, 2.97)	2.86	(2.40, 3.41)	3.90	(3.51, 4.34)	2.86	(2.47, 3.32)
Lung and Bronchus	2.47	(2.39, 2.55)	2.57	(2.42, 2.72)	2.93	(2.75, 3.13)	2.79	(2.62, 2.98)
Pancreas	2.71	(2.55, 2.89)	2.70	(2.47, 2.94)	3.14	(2.90, 3.40)	2.67	(2.43, 2.93)
Colorectal	2.90	(2.75, 3.06)	2.62	(2.40, 2.87)	3.28	(3.07, 3.52)	2.35	(2.15, 2.57)
Kidney/Renal Pelvis	3.22	(2.92, 3.54)	2.18	(1.76, 2.71)	3.08	(2.70, 3.53)	2.28	(1.95, 2.68)
Brain	2.25	(2.05, 2.48)	1.91	(1.70, 2.16)	2.18	(1.93, 2.46)	2.16	(1.89, 2.48)
Stomach	2.83	(2.59, 3.09)	2.44	(2.10, 2.84)	2.70	(2.37, 3.07)	2.15	(1.85, 2.50)
Myeloma	2.33	(2.05, 2.64)	1.86	(1.52, 2.28)	2.70	(2.32, 3.15)	1.44	(1.19, 1.75)

CAT (Type) was entered as a time dependent covariate, comparison was with no CAT

Limitations and Strengths of the Analysis

Limitations:

- Reliance on hospital discharge coding for Dx of CAT events.
- Specifics regarding chemotherapy treatment were not available in data.
- Could not discern 'incidental PE' from 'symptomatic PE'.

Strengths:

- Population based (all patients hospitalized in public hospitals in Calif.)
- Based on Comprehensive Cancer Registry Data and National Death Registry.
- Temporally linked hospital/ED records,

Conclusions

- The previously reported incidence of CAT has increased significantly from the early 1990's, particularly the diagnosis of PE.
- Calf-vein thrombosis alone is a significant independent predictor for reduced survival.
- Adjustment for the competing risk of death has lowered our prior estimate of the incidence of CAT in advanced stage patients.
- CAT is consistently more likely in African-Americans; less likely in Asians. Thus, cancer does not change the relative incidence of VTE among races.
 - In diverse populations, CAT risk scores should include race/ethnicity.



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Thank you