SUPPLEMENTAL MATERIALS

Supplemental Methods

National inpatient sample dataset (NIS)

The National Inpatient Sample (NIS) is an inpatient database in the United States (1) developed by the Agency for Healthcare Research and Quality (AHRQ). It comprises of 20% sample of all inpatient discharges from US hospital excluding patients admitted in observation status, short-term rehabilitation hospitals, long-term non–acute care hospitals, psychiatric hospitals, and alcoholism or chemical dependency unit. The dataset contains deidentified information regarding each hospitalization, including demographic characteristics, comorbidities, discharge diagnoses, procedures, outcomes, and cost of hospitalization. In the present study, we used data for the years January 1, 2003 through September 30, 2015. The design of the NIS changed twice during the study period.(2) Between 2007 and 2011, the NIS comprised all inpatient discharges (100%) from a random 20% sample of acute-care hospitals in the United States. However, in 2012, instead of including all discharges from a 20% sample of hospitals, the database was constructed using a systematic sampling of 20% of discharges from all (100%) hospitals stratified by hospital, census division, ownership status, urban vs rural location, teaching status, and bed size, as well as patient diagnosis-related group and admission month. To facilitate patient-level trend analysis, a new set of weights called “trendwt” were developed for data for previous years (1993-2011).(1, 3) The trend weights replaced the original NIS discharge weights for trend. Trend weights should be used for all patient and hospital level analyses.(3) In 2015, NIS moved to International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM)

based data collection and hence data was available only till September 2015.(4) Data collection methodology was unchanged compared to 2012.

Specific data elements in the NIS includes demographics (age, sex, race), income quartile, insurance status, hospital level characteristics, comorbidities, various secondary diagnoses used to identify in hospital outcomes and discharge disposition. In 2015, the Healthcare Cost and Utilization Project (HCUP) State Inpatient Databases was used to create two validated indices designed to predict in-hospital mortality (morscore) and 30-day readmission, based on the aforementioned 29 comorbidities measures.(5) These 2 indices were calculated for our cohort as well.

Charges and length of stay were log-transformed (natural log) because they are not normally distributed, and geometric means were presented.(6, 7) The actual hospitalization cost is obtained by multiplying hospital charges with cost-to-charge ratios(8) and the wage index for each hospital over a given year. The wage index helps correct for geographic variations in costs among hospitals.(8) For length of stay as 0 days, a value of 0.0001 were imputed to avoid negative log values.

National Readmission Dataset (NRD)

NRD is a nationally representative rehospitalization dataset developed by AHRQ.(1) It has been constructed using discharge-level data for all hospitalizations from State Inpatient Databases of geographically dispersed participating states (18-27 states during 2010-2015).(1) The NRD contains a de-identified unique patient linkage number, which allows for the determination of readmissions by

tracking of patients across hospitals within a calendar year. However, the patients cannot be tracked across years and there is no linkage with NIS data. For this study we utilized 2013 and 2014 NRD datasets.

For a 30-day readmission follow up, only patients who presented in the first 11 months (December excluded) of the year can be included. Similarly, for a 90-day readmission follow up, only patients who presented in the first 9 months (October to December excluded) of the year can be included. Data elements utilized in NRD were the primary DXCCS discharge diagnosis. List of all discharge diagnoses were created using DXCCS1 using the list of CCS codes provided in a recent paper by Kwok CS, et al.(9)

Cohort Creation

Once the initial NIS cohort of AIS patients were identified using the ICD-9 CM and CCS codes as described in the manuscript, consistent with prior studies, we excluded patients with ICD-9-CM codes for rehabilitation (V57), trauma (800, 801, 802, 803, 804, 850, 851, 852, 853, 854), due to their confounding influence of tPA outcomes and contraindication to tPA administration.(10) Similarly, as the likelihood of identifying an appropriate stroke diagnosis increases when a known risk factor for stroke is added to the primary diagnosis, we considered AIS risk factors for further event validation.(11) Specifically, we checked for the presence of at least one secondary diagnosis (DX2-DX30), including hypertension, diabetes, smoking, coronary artery disease, chronic kidney disease, prior ischemic stroke, peripheral vascular disease, atrial fibrillation, obesity, alcoholism and hyperlipidemia. Only those admissions which met the primary and secondary diagnosis criteria entered the study. Accordingly, within this newly created cohort, we identified the cancer patients using DXCCS codes (DXCCS1-DXCCS30) 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29,

30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45. Primary gastrointestinal malignancies (DXCCS 12-15), primary CNS malignancies (DXCCS 35) and hematologic malignancies (DXCCS 37-40) were excluded in a sensitivity analysis to exclude cancers with higher bleeding risk.

NIS and NRD provide 29 comorbidities (also known as Elixhauser's Comorbidity measures) which are generated using ICD-9 CM diagnoses and the diagnosis-related group which was in effect on the day of discharge [12]. These comorbidities are not directly related to the principal diagnosis or the main reason for admission and are likely to have originated before the hospital stay [13]. These comorbidities were also used to identify cancer diagnosis.

Variance analyses

Annual variance analyses for the NIS datasets created were performed using the DOMAIN method for all years, as described in pre and post -2012 AHRQ methods, to ensure that the estimated statistics and measures of variance were accurate(14, 15). Similarly, the DOMAIN method was used for the 2013-2014 NRD dataset to ensure accurate estimates and variance.(16) We followed the recommendations from AHRQ for analysis using survey data.(17, 18)

Active Cancer Therapy

In addition, to better understand the potential impacts of cancer treatments on the decision for tPA use, we performed subgroup analysis, by coded active anticancer therapy status. Chemotherapy was identified using ICD-9-CM codes 99.25, V58.1, V66.2, or V67.2 for those with available codes. Similarly, radiotherapy was identified using ICD-9-CM diagnosis codes V58.0, V66.1, and

V67.1, ICD-9-CM procedure codes 92.2-92.39. However, less than 1% (1,010) of the patients had the aforementioned codes (compared to 564,722 patients who had AIS with a cancer diagnosis, but no treatment code). This is most likely influenced by the traditional coding of most of these therapies under outpatient administration, as well as preferential use of procedural terminology-4 and revenue center codes, rather than ICD-9 for anticancer therapy care.(19)

Propensity Matching

We used an unfitted multivariable logistic regression model to determine each admissions' propensity of having cancer. Age, gender, race, insurance status, hypertension, diabetes, HCUP mortality score, as well as location, teaching status, size and geographic region of the hospital were used in the propensity estimation model. The propensity score, generated by logistic regression, represents the relationship between multiple characteristics and the dependent variable as a single characteristic. The propensity score thus obtained (between 0 and 1) is utilized by an 8®1 Digit Match algorithm which matches a case to control at the 8th decimal point followed by 7th decimal point followed by 6th decimal point and so on using a greedy matching algorithm.(20) We then matched 5 non-cancer:1 cancer admission (5:1 match). Higher number of controls (5:1) were matched because there were significantly smaller cancer admissions than non-cancer admissions. In another sensitivity analysis SASI score was added to the aforementioned model.

Exploratory Multivariable Logistic Regression Model

These analyses were performed using forward regression using an entry p value of <0.01 was utilized to express the outcomes of overall among all patients. The exit-α was set at 0.05. Variables utilized for this model included potentially confounding demographic,

economic, CVD, cancer, and hospital characteristics. Total Elixhauser's variables, morscore, and HCUP readmission score were excluded from the final model to avoid repeat adjustment using derived variables. The c-score of the model was 0.76. Subsequent sensitivity analysis of the model was performed using calculated E-values for significant odds ratios ($p < 0.05$).[21] Variables which had an E-value ≥ 1.3 and E-confidence interval of ≥ 1.3 shows associations beyond unmeasured bias.

Figure S1A – Adjusted trends in thrombolytic utilization during stroke hospitalization among subjects with concomitant cancer (excluding primary CNS, gastrointestinal, and hematologic malignancies) and non-cancer. Presented per 1000 stroke hospitalizations. $P_{\text{cancer vs non-cancer}}$ = 0.29 (2003-2015) and $P_{\text{cancer vs non-cancer}}$ in post 2012 cohort = 0.0001.

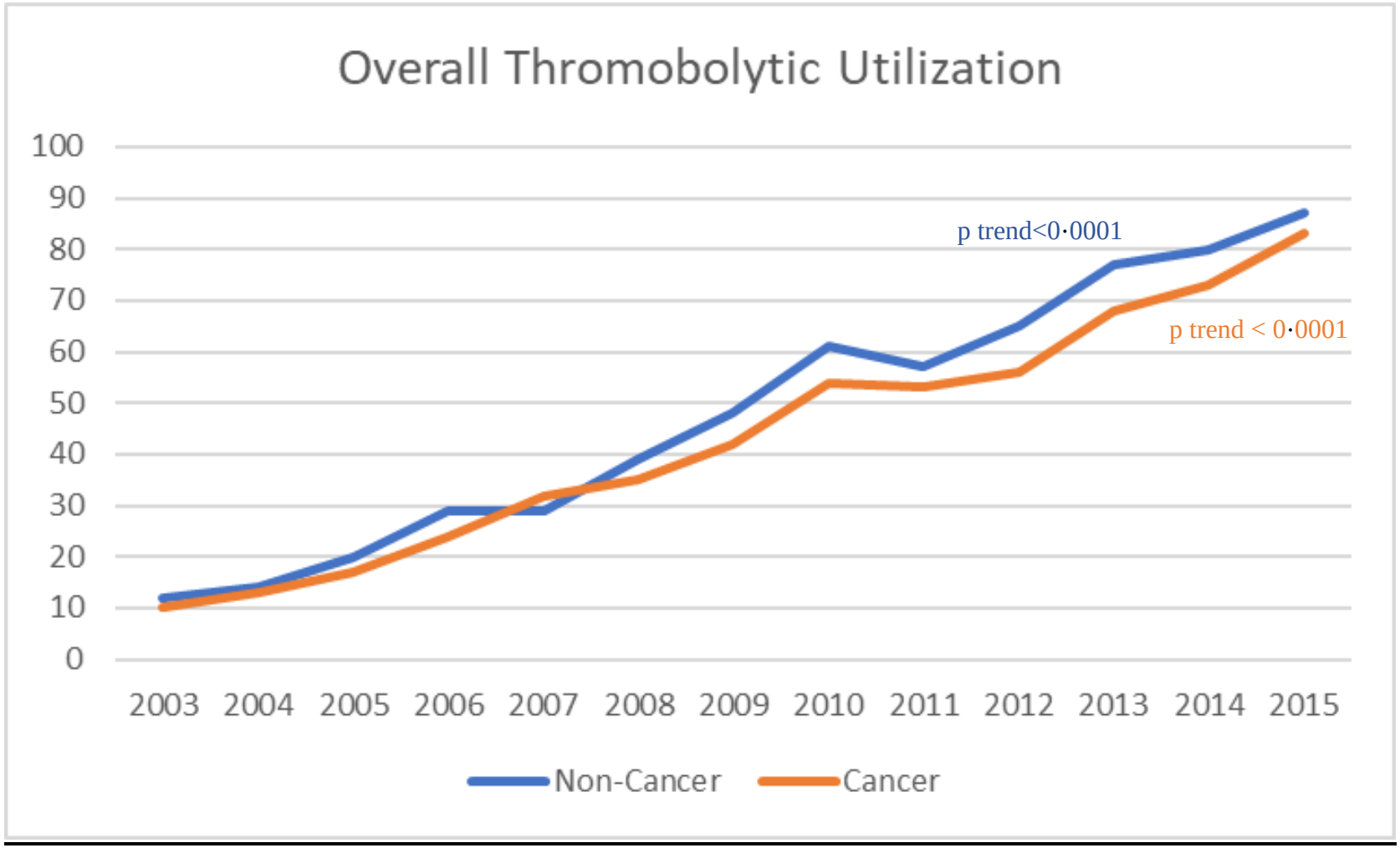
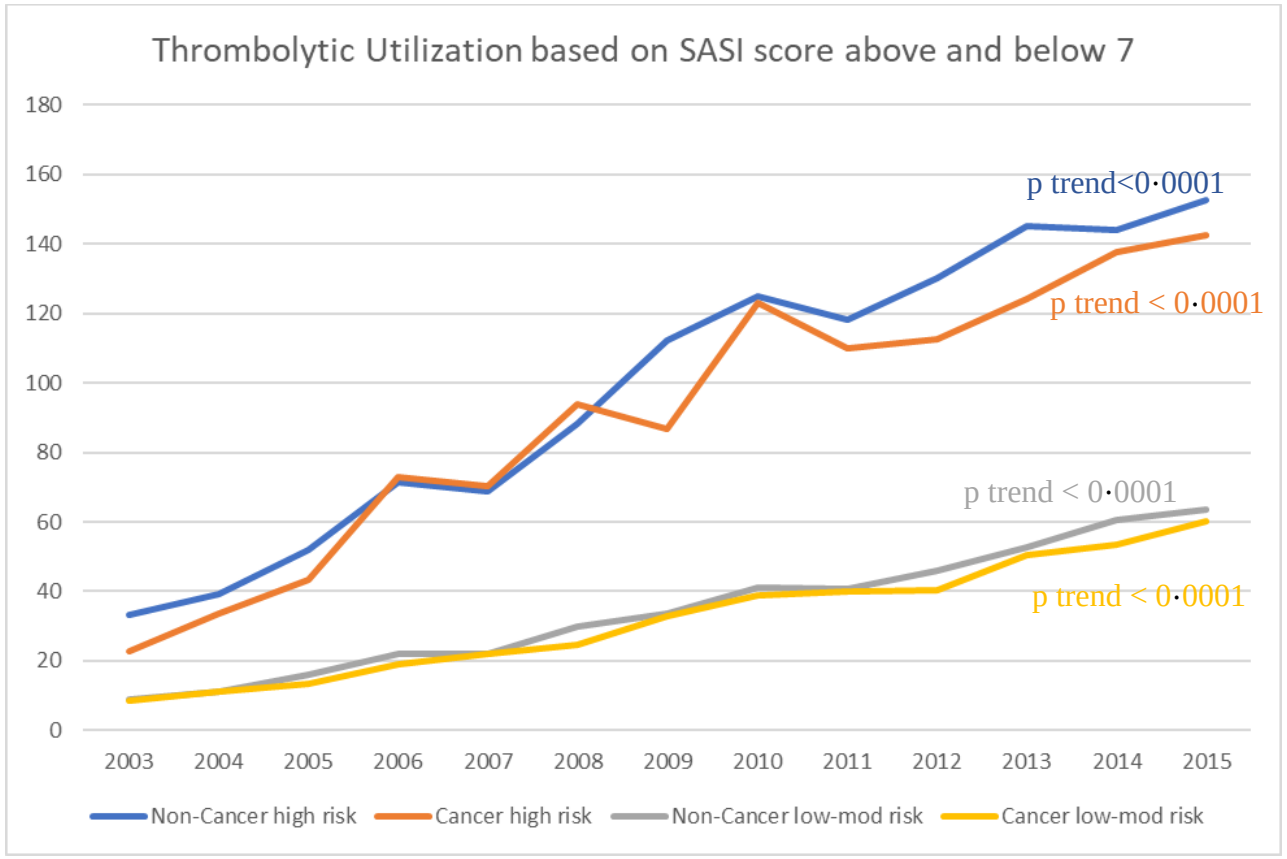


Figure S1B

i – Adjusted trends in thrombolytic utilization stratified by SASIscore ≥/< 7. Presented per 1000 stroke hospitalizations. $P_{\text{cancer vs non-cancer}}$ (SASI < 7) = 0.77; $P_{\text{cancer vs non-cancer}}$ (≥ 7) = 0.61.

ii – SASIscore adjusted (above 8 adjustments plus SASI score). Presented per 1000 stroke hospitalizations. $P_{\text{cancer vs non-cancer}}$ = 0.71.

i.



ii.

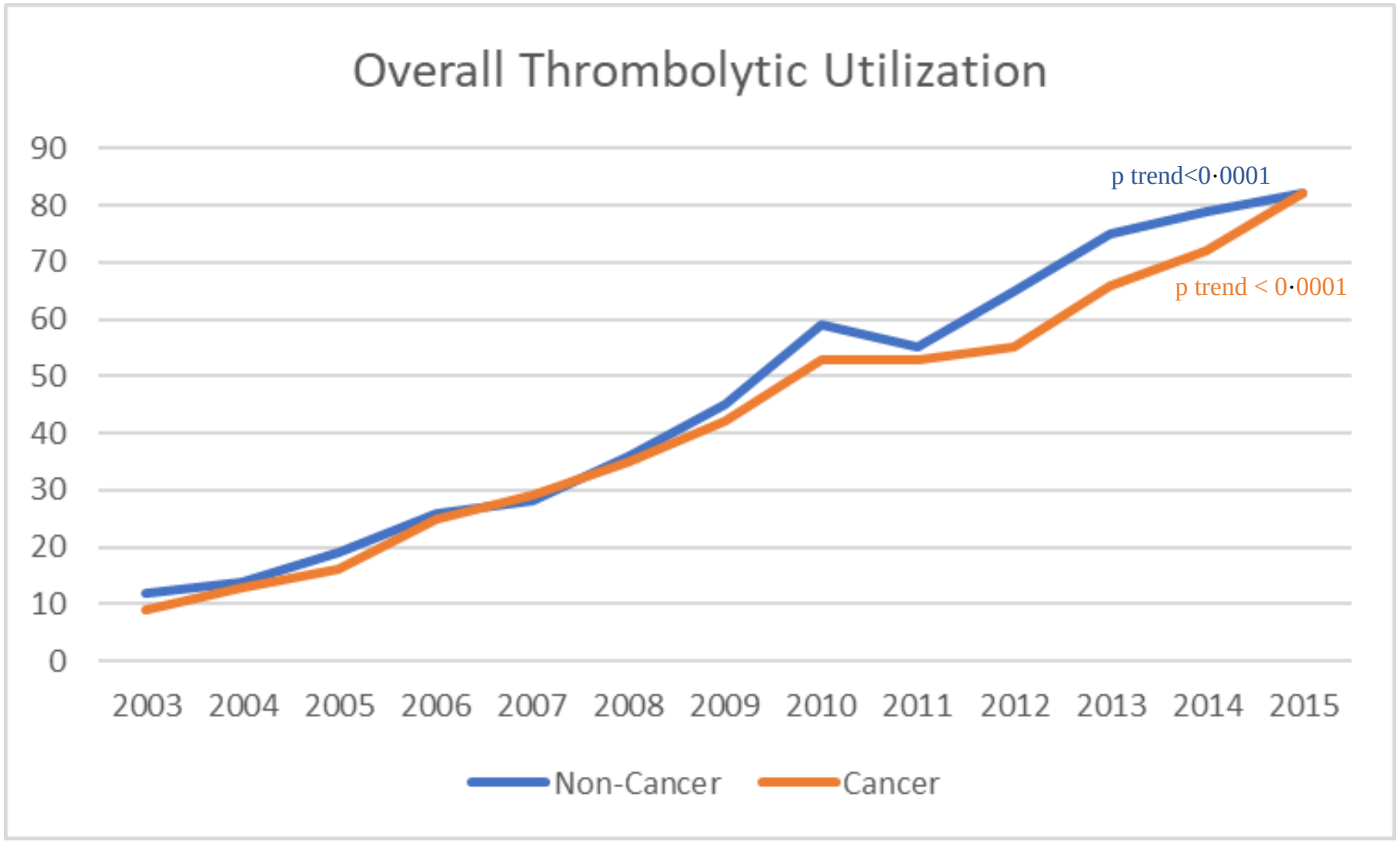

Overall Thrombolytic Utilization
90
80
70
60
50
40
30
20
10
0
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
p trend<0·0001
p trend < 0·0001
Non-Cancer
Cancer

Figure S1C – Adjusted trends in thrombolytic utilization during stroke hospitalization between sexes. Presented per 1000 stroke hospitalizations. All p-trends < 0.0001. $P_{\text{cancer vs non-cancer}}$ (male) < 0.0001; $P_{\text{cancer vs non-cancer}}$ (female) = 0.23.

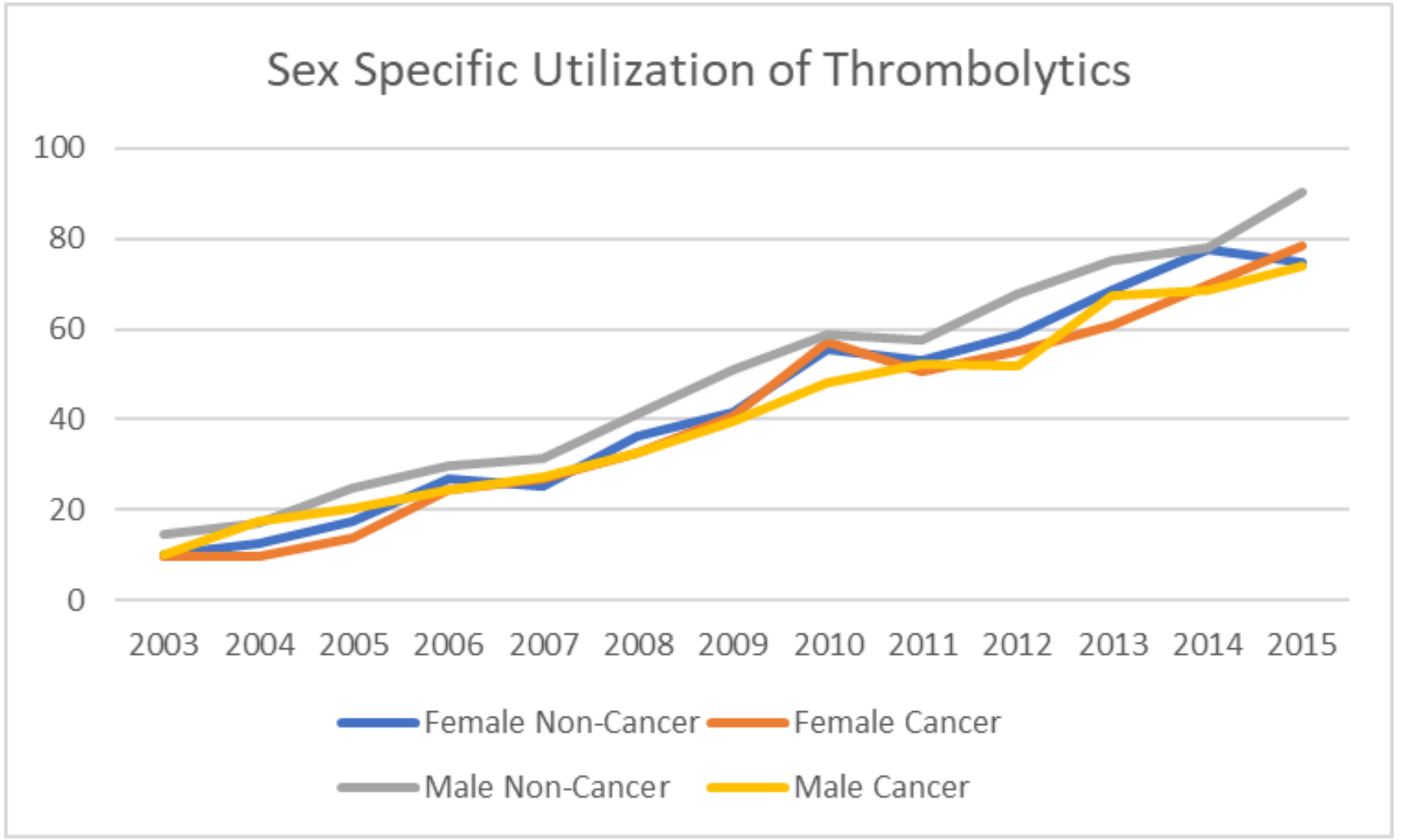


Figure S1D – Adjusted trends in thrombolytic utilization during stroke hospitalization in patients < 50 years of age. Presented per 1000 stroke hospitalizations. $P_{\text{cancer vs non-cancer}} = 0.52$.

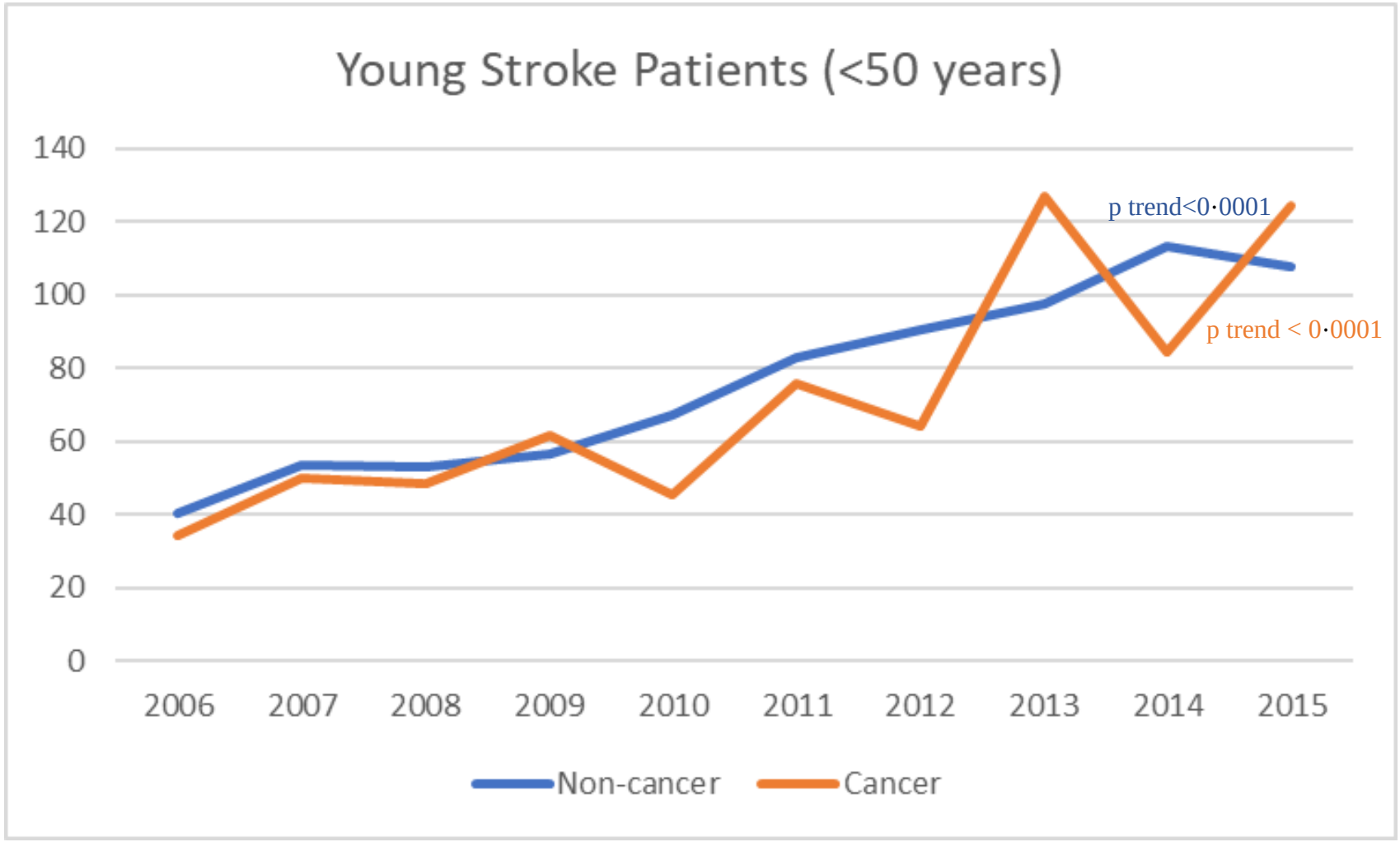


Figure S2A Intracranial hemorrhage adjusted trends with and without thrombolytic therapy. Presented as per 1000 stroke patients.

$P_{\text{cancer vs non-cancer}}$ (thrombolytic) = 0.87; $P_{\text{cancer vs non-cancer}}$ (non-thrombolytic) = 0.70.

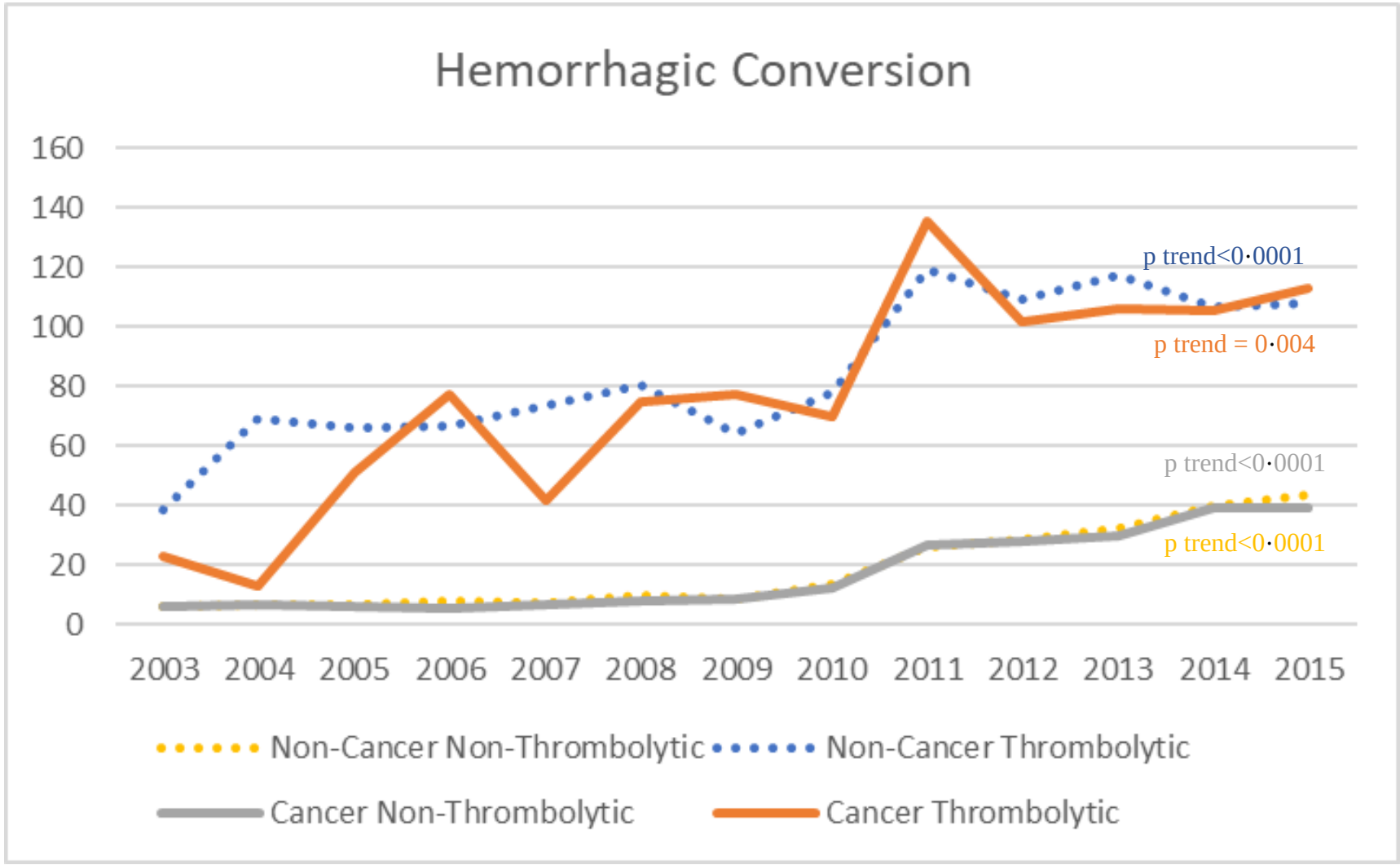


Figure S2B All-cause bleeding adjusted trends with and without thrombolytic therapy. Presented as per 1000 stroke patients. $P_{\text{cancer vs non-cancer}}$ (thrombolytic) = 0.94; $P_{\text{cancer vs non-cancer}}$ (non-thrombolytic) = 0.02.

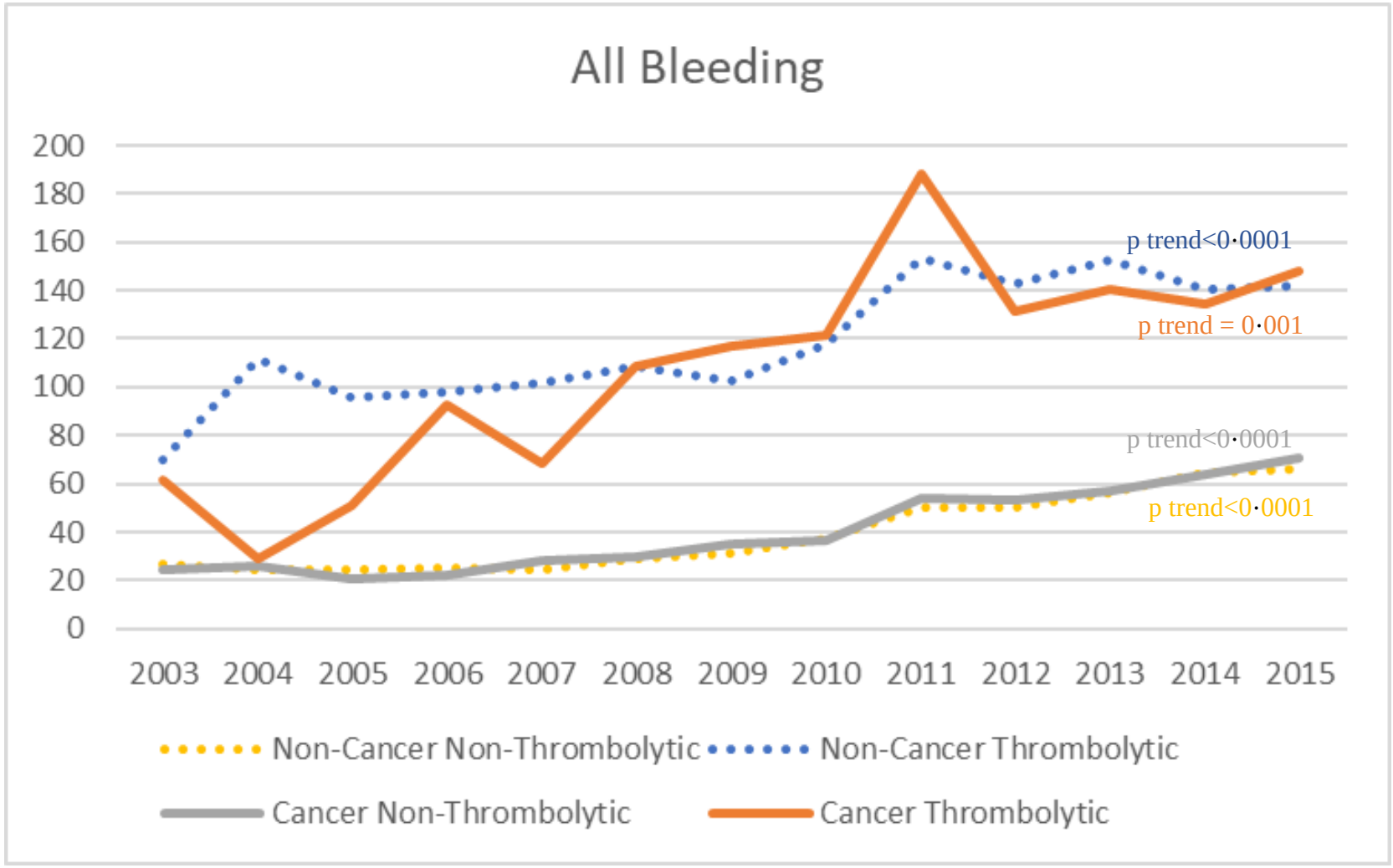
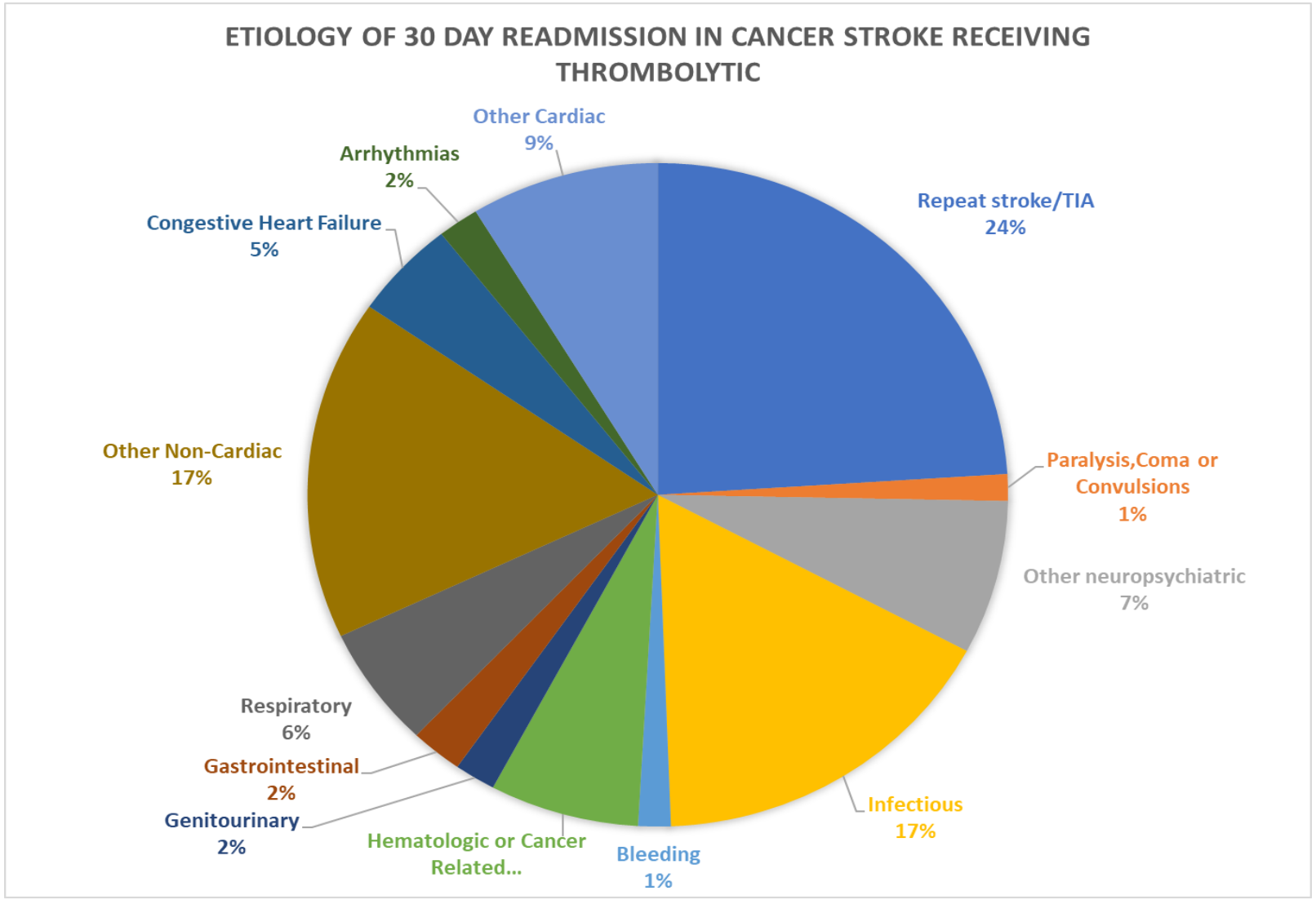


Figure S3 Causes of 30-day readmission post thrombolytic therapy in cancer and non-cancer hospitalizations (calculated annually and averaged for years 2013 and 2014).



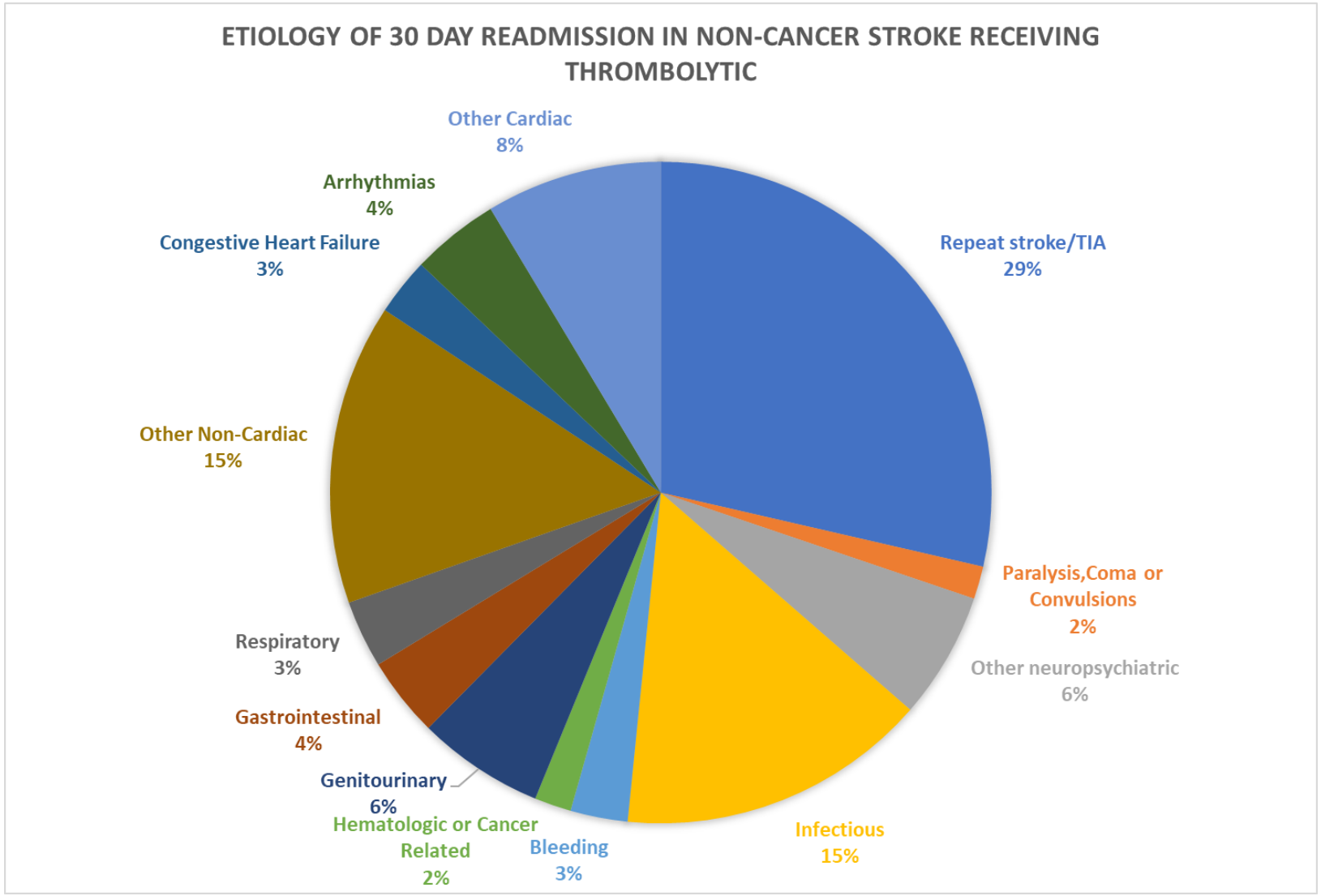
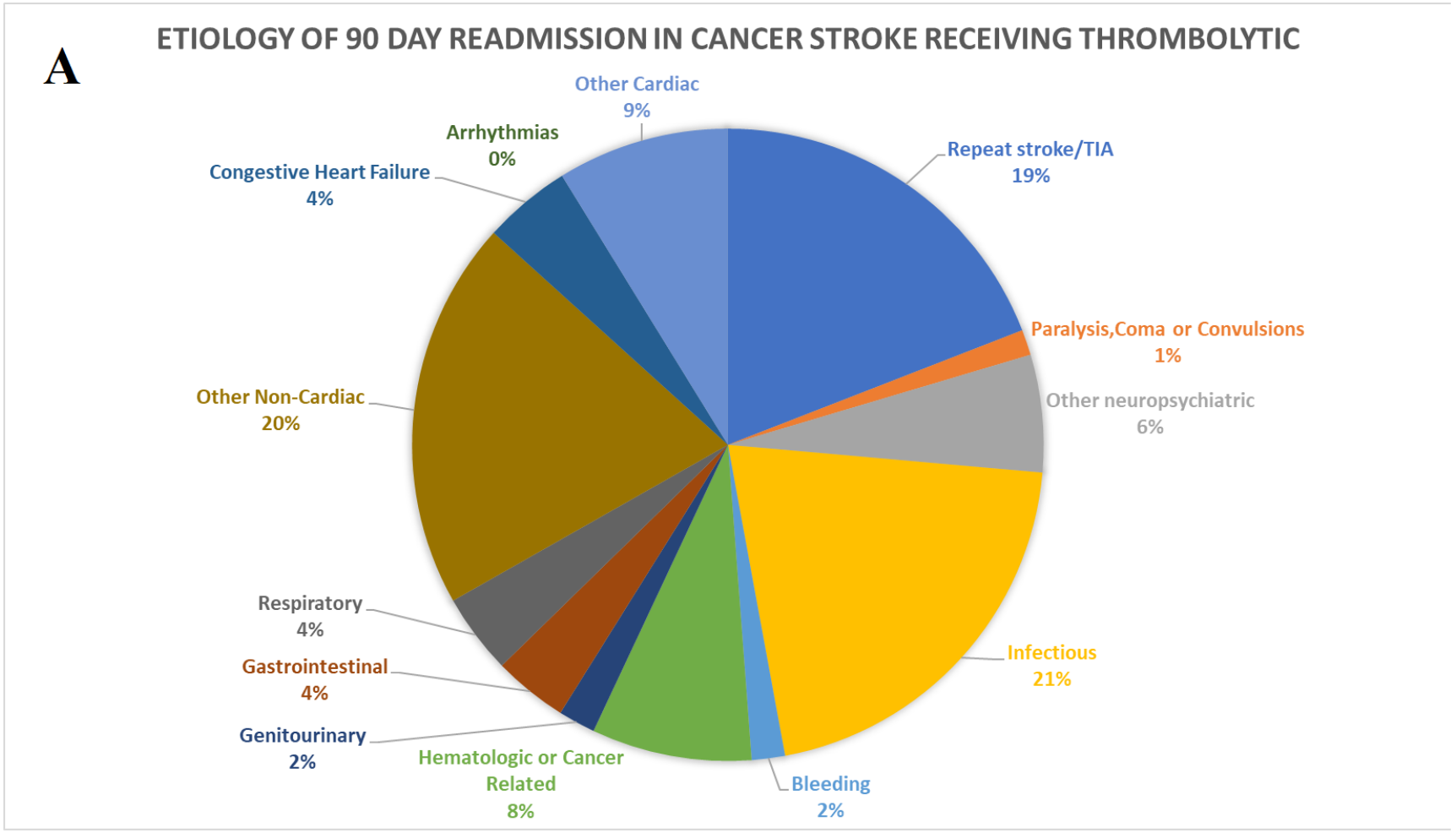

ETIOLOGY OF 30 DAY READMISSION IN NON-CANCER STROKE RECEIVING THROMBOLYTIC
Other Cardiac 8%
Arrhythmias 4%
Congestive Heart Failure 3%
Repeat stroke/TIA 29%
Other Non-Cardiac 15%
Paralysis,Coma or Convulsions 2%
Other neuropsychiatric 6%
Respiratory 3%
Gastrointestinal 4%
Genitourinary 6%
Hematologic or Cancer Related 2%
Bleeding 3%
Infectious 15%

Figure S4 - Causes of 90-day readmission post thrombolytic therapy by presence/absence of cancer (**A** and **B**; calculated annually and averaged for years 2013 and 2014).



B

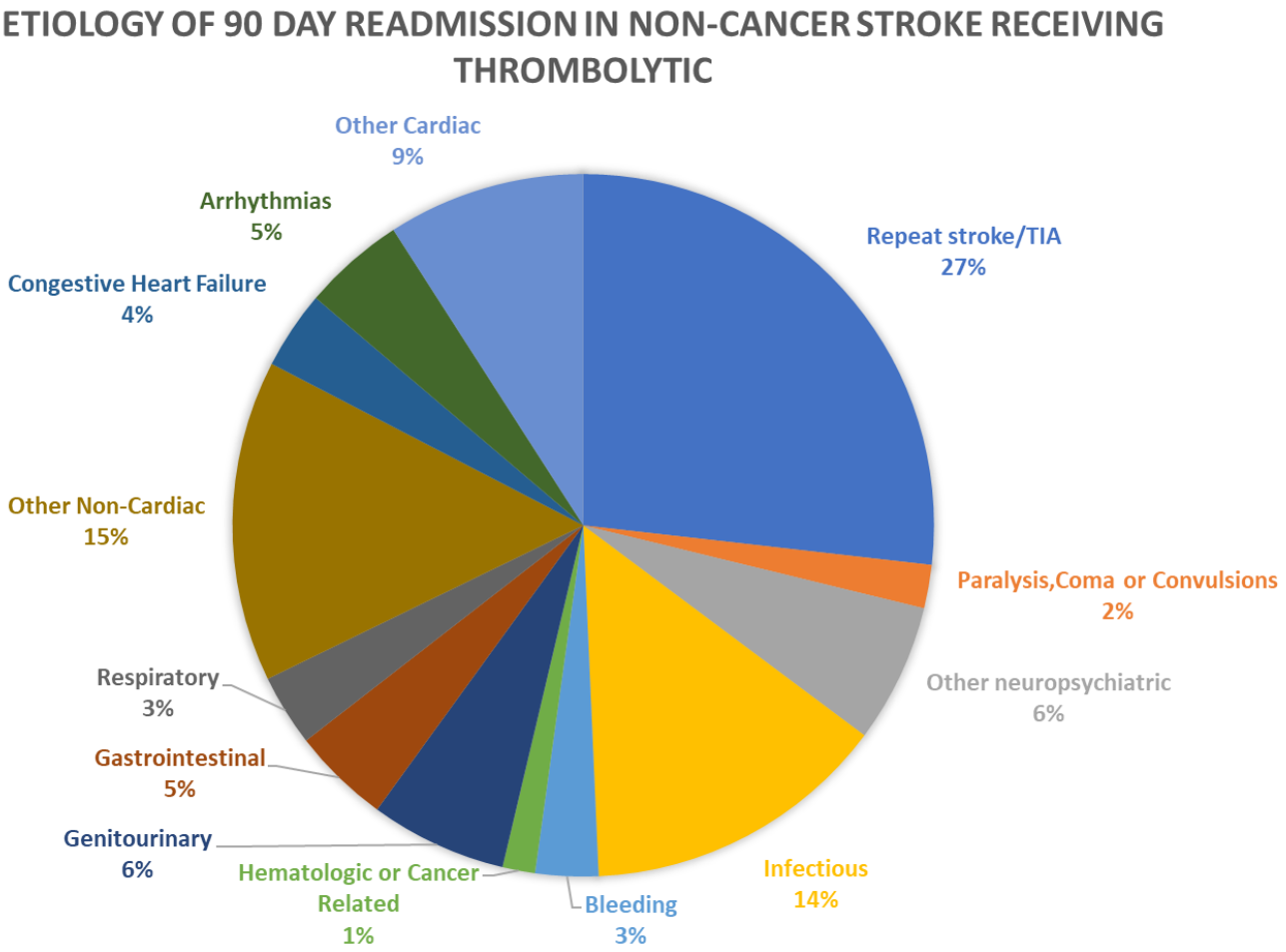

ETIOLOGY OF 90 DAY READMISSION IN NON-CANCER STROKE RECEIVING THROMBOLYTIC
Other Cardiac 9%
Arrhythmias 5%
Congestive Heart Failure 4%
Other Non-Cardiac 15%
Respiratory 3%
Gastrointestinal 5%
Genitourinary 6%
Hematologic or Cancer Related 1%
Bleeding 3%
Infectious 14%
Other neuropsychiatric 6%
Paralysis,Coma or Convulsions 2%
Repeat stroke/TIA 27%

Figure S5 - Flow chart showing methods

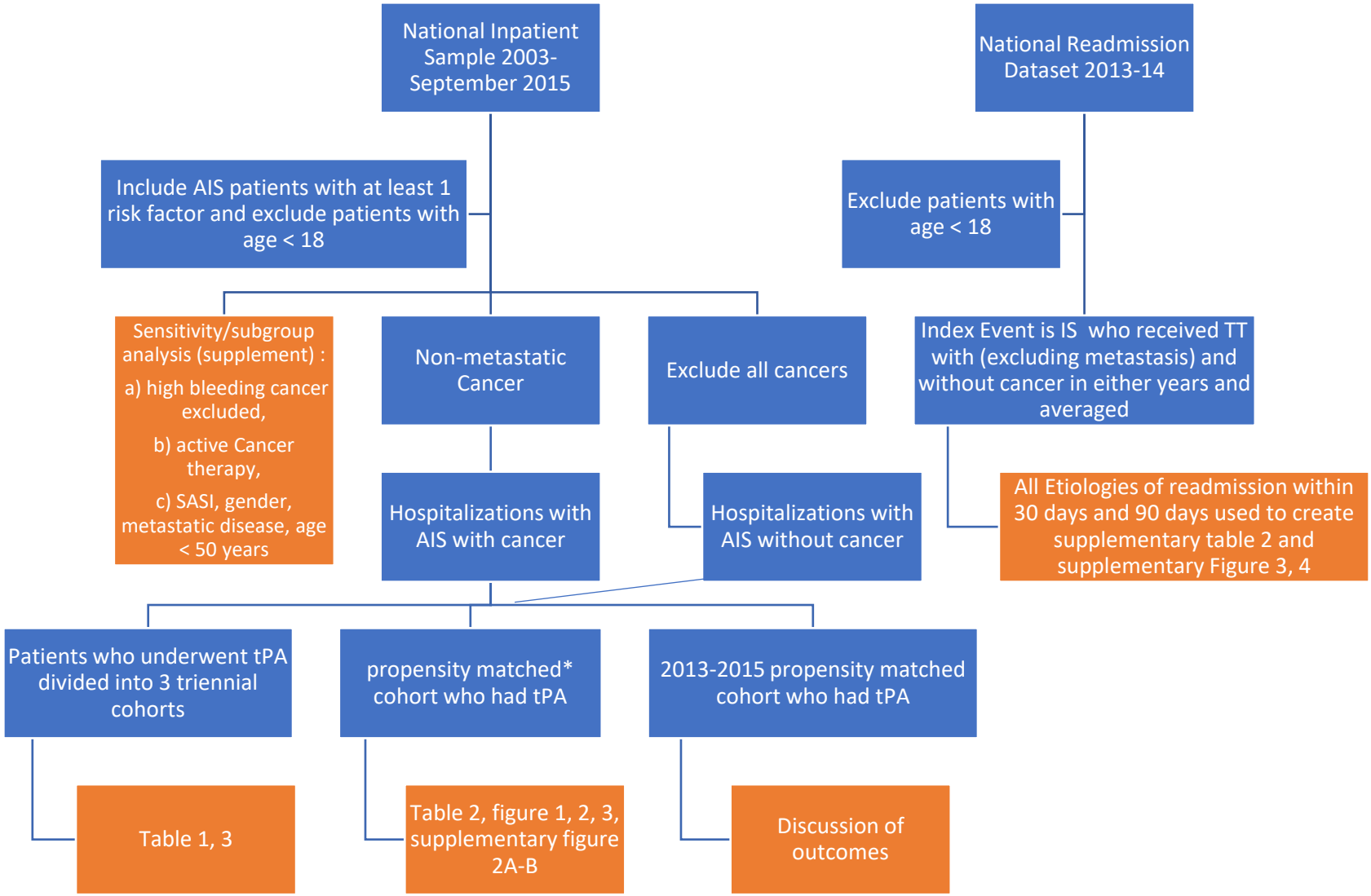


Table S1. Standardized differences presented from current table 1 variables

	2003-2005			2008-2010			2013-2015*		
	Cancer (n=1,316)	**Non-Cancer (n=15,444)**	**Standardized differences**	**Cancer (n=5,715)**	**Non-Cancer (n=47,610)**	**Standardized differences**	**Cancer (n=11,750)**	**Non-Cancer (n=83,375)**	**Standardized differences**
Patient Characteristics									
Age, years (mean ± SE)	73.2 ± 0.7	66.8 ± 0.3	0.45	74.4±0.4	67.5±0.2	0.47	74.2 ± 0.3	67.2 ± 0.1	0.48
Women, %	44.9	46.9	-0.03	51	49.7	0.02	49.8	49.4	0.006
Race, %			0.24			0.19			0.25
White	83.9	76		79.8	72.7		79.7	69.2	
Black	7.9	12.9		11.9	14.8		10.3	15.6	
Hispanic	4.5	6.2		4.1	6.5		5	8.6	
Asian or Pacific Islander	1	2.4		1.3	2.8		2	3.3	
Native American	0	0.1		0.3	0.4		0.2	0.3	
Other	2.8	2.3		2.6	2.9		2.6	3	
Income quartiles‡			0.17			0.14			0.14
0-25	18.5	23.3		19.2	25		22.5	28.2	
26-50	24.6	25.9		26.7	25.1		24.9	25.2	
51-75	25.7	26.1		25.9	24.9		26.1	24.2	
76-100	31.2	24.7		28.2	25		26.4	22.4	
Payment source (%)			0.47			0.41			0.36
Medicare	78.7	58.7		76.6	58.9		77.3	61.3	

Medicaid	2.5	5.6		4.3	7.2		3.8	8.7	
Private	17.3	28.4		15.5	25.9		15.1	22.4	
Self-Pay	0.7	4.8		1.3	4.9		2.2	4.8	
No Charge	0	0.4		0.4	0.5		0.2	0.4	
Others	0.8	2.1		2	2.5		1.5	2.4	
Comorbidities (%)									
Stroke Specific									
Prior Stroke	0[§]	0[§]		11.6	8.9	0.1	14.3	12.7	0.05
Hypertension	77.6	76.7	0.02	82	81.4	0.01	84.4	84.6	-0.003
Diabetes	21.2	23.9	-0.07	31.6	30.7	0.02	32	36.2	-0.09
Obesity	1.9	5.7	-0.2	6.5	9..3	-0.1	9.5	13.6	-0.13
Hyperlipidemia	22.4	24.6	-0.05	42	42.3	-0.009	54.8	53.8	0.02
Chronic Kidney Disease	1.8	4	-0.13	11.8	10.1	0.05	17.1	13	0.12
Coronary Artery Disease	30.7	28.6	0.04	32.1	29.3	0.06	33.1	28.4	0.10
Atrial Arrhythmia	31.6	31.8	0.0008	41.5	34.7	0.14	38.9	32.2	0.14
Peripheral Vascular Disease	5.6	7.4	-0.09	9.1	9.1	0.003	10.5	9.9	0.02
Alcoholism	3.3	4.3	-0.06	2.3	4.4	-0.11	3.3	5.1	-0.09
Smoking	20.8	21.3	-0.01	26.4	27.1	-0.01	36.2	34.5	0.04
Other Cardiovascular									
Congestive Heart Failure	12.4	16	-0.10	15.8	16.4	-0.01	17.3	16.6	0.02

Valvular Heart Disease	7.2	11.4	-0.14	11.5	10.2	0.04	13.1	10.8	0.07
Non-Traditional									
Weight Loss	1.5	1.7	-0.01	3.3	3.6	-0.01	3.9	3.4	0.03
Anemia	0.7	0.5	0.03	0.1	0.2	-0.007	1.4	1.4	0.004
Arthritis and Collagen Vascular disease	2.5	1.9	0.04	1.8	1.1	-0.03	3.3	2.6	-0.005
Chronic liver disease	0	0.5	-0.10	0.6	0.8	-0.02	1	1.3	-0.02
Chronic lung disease	13.2	14	-0.02	15.9	14.1	0.05	19.5	15.2	0.11
Hypothyroidism	8.7	8.7	-0.001	15.3	12	0.1	18	14	0.11
Psychiatric	7.5	6.5	0.05	9.1	10.1	-0.03	13	12.9	0.003
Fluid/electrolyte disorder	13.8	14.9	-0.04	19.6	20.6	-0.02	22.9	21.8	0.02
Coagulation disorder	2.2	2	0.01	3	2.7	0.02	5.6	3.6	0.09
Substance abuse	4.1	5.4	-0.07	3.1	5.8	-0.13	4.3	7.6	-0.14
Total Elixhauser's comorbidities ≥ 3	36.6	35.5	0.06	66.5	59.9	0.13	70.9	65.8	0.12
Elixhauser's readmission score (mean ± SE)	9.8 ± 0.6	8.6 ± 0.2	-0.10	17±0.4	14±0.2	0.22	18.8 ± 0.3	15.2 ± 0.1	0.24
Elixhauser's mortality score (mean ± SE)	3.8 ± 0.4	3.2 ± 0.2	0.11	7.9±0.3	6.5±0.2	0.16	8.6 ± 0.2	6.4 ± 0.1	0.22

SASI Score (mean ± SE)	5.4 ± 0.4	5.5 ± 0.2	0.06	6.1±0.2	6.6±0.2	0.16	6.6 ± 0.1	6.6 ± 0.1	0.22
Hospital Level Variables									
Teaching hospital (%)	59.3	52.9	0.12	56.6	58	-0.02	69.1	69.1	-0.0006
Bed size, (%)			0.04			0.05			0.02
Small	5.8	5.4		5.4	4.6		10	9.7	
Medium	17.6	19.3		21.5	20.7		27	27.7	
Large	76.5	75.3		73.1	74.7		63	62.7	
Region (%)			0.35			0.07			0.11
Northeast	22.6	18.1		22.5	21.8		18.7	17.6	
Midwest	26.3	25.1		22.3	20.1		22.1	20.6	
South	24.1	39.2		35.1	37.9		34.9	40	
West	27.1	17.6		20.1	20.2		24.3	21.8	
Hospital in urban location, (%)	93.7	92.8	0.03	96.4	94.4	0.1	96.3	96.7	-0.02
Weekend admission (%)	25.3	28.2	-0.06	26.4	27.8	-0.04	25.2	27.3	-0.05

Table S2A. Multivariable model of predictors of in-hospital mortality in the 2013-2015 entire cohort (c= 0.85) and comorbid cancer cohort (c=0.84) receiving thrombolytics.

Entire Cohort who received thrombolytics						
	Odds-Ratio	**95% Confidence Interval**		**p-value**	**E-value***	**E-Value of Confidence Interval***
Patient Characteristics		Lower Limit	Upper Limit			
Age						
18 – 39 years	1					
60 – 79 years	2	1.1	3.6	0.02	2.2	1.3
≥ 80 years	3.6	2	6.5	<0.0001	3.2	2.1
Comorbidities						
Cancer	1.2	1	1.4	0.06†		
Prior Stroke	1	0.8	1.1	0.6†‡		
Congestive Heart Failure	1.5	1.2	1.7	<0.0001	1.7	1.5
Coronary Artery Disease	1.2	1	1.2	0.02§	1.4	1.1
Peripheral Vascular Disease	1.4	1.1	1.7	0.002	1.6	1.3
Chronic Kidney Disease	1.1	1	1.2	0.02§	1.5	1.2
Atrial Arrhythmia	1.4	1.2	1.6	<0.0001	1.7	1.4
Fluid/electrolyte disorder	1.3	1.1	1.5	0.002	1.5	1.3
Coagulation disorder	1.5	1.2	2.0	0.003	1.8	1.4
SASI	1.2	1.1	1.2	<0.0001	1.4	1.3
In-hospital Outcome						
Intracranial hemorrhage	3	2	4.5	<0.0001	2.9	2.2
GI bleeding	1.5	0.9	2.5	0.1†		
All Bleeding	1.1	0.7	1.7	0.6†		
Cancer Cohort who received thrombolytics‖						
Hispanic vs white race	0.3	0.1	0.8	0.02	3.5	1.6
Comorbidities						
Prior Stroke	1.1	0.7	1.6	0.7†		
Congestive Heart Failure	1.3	0.8	2	0.3†		
Coronary Artery Disease	1.4	0.9	2.1	0.1†		

Chronic Kidney Disease	1.5	1	2.2	0.05[§]	1.7	1.1
Atrial Arrhythmia	1	0.7	1.5	0.9[†]		
Coagulation disorder	2.5	1.4	4.4	0.002	2.5	1.6
SASI	1.2	1.1	1.2	<0.0001	1.4	1.3

* Variables which had an E-value ≥ 1.3 and E-confidence interval of ≥ 1.3 show associations beyond unmeasured bias

[†] E-value not calculated for not significant variable

[‡] Univariable OR presented as the variable did not meet the criteria of 0.001 to enter the multivariable model

[§] E-value < 1.3 shows that the result of this test can be explained away by biases and does not meet the sensitivity cut-point

[‖] None of the in-hospital outcomes mentioned above were significant

Table S2B. Multivariable model of combined outcome predictors (bleeding and in-hospital mortality) in the 2013-2015 entire cohort (c= 0.76) and comorbid cancer cohort (c=0.74) receiving thrombolytics.

Entire Cohort who received thrombolytics						
	Odds-Ratio	**95% Confidence Interval**		**p-value**	**E-value***	**E-Value of Confidence Interval***
Patient Characteristics		Lower Limit	Upper Limit			
Age						
18 – 39 years	1					
60 – 79 years	1.6	1.1	2.2	0.01	1.8	1.3
≥ 80 years	2	1.3	2.8	0.0004	2.1	1.6
Comorbidities						
Cancer	1.1	0.9	1.2	0.32†		
Prior Stroke	0.9	0.8	1.1	0.20†		
Congestive Heart Failure	1.1	1.0	1.2	0.26†		
Coronary Artery Disease	1.2	1.1	1.3	0.003	1.4	1.2§
Chronic Kidney Disease	1.1	1	1.2	0.11†		
Atrial Arrhythmia	1.5	1.3	1.6	<0.0001	1.7	1.6
Coagulation disorder	1.8	1.5	2.2	<0.0001	2	1.8
SASI	1.1	1.1	1.1	<0.0001	1.3	1.3
Cancer Cohort who received thrombolytics						
African American vs white race	0.6	0.4	0.9	0.02	1.9	1.3
Comorbidities						
Prior Stroke	1.0	0.8	1.4	0.8†‡		
Congestive Heart Failure	0.9	0.6	1.2	0.49†		
Coronary Artery Disease	1.3	1	1.6	0.08†		
Chronic Kidney Disease	1.2	0.9	1.7	0.35†		
Atrial Arrhythmia	1.3	1.1	1.9	0.001	1.8	1.4
Coagulation disorder	1.8	1.2	2.8	0.007	2.1	1.4
SASI	1.1	1.1	1.1	<0.0001	1.3	1.3

* Variables which had an E-value ≥ 1.3 and E-confidence interval of ≥ 1.3 show associations beyond unmeasured bias

† E-value not calculated for not significant variable
‡ Univariable OR presented as the variable did not meet the criteria of 0.001 to enter the multivariable model
§ E-value shows that the result of this test can be explained away by biases and does not meet the sensitivity cut-point

Table S3. Difference in readmission etiologies in cancer vs non-cancer hospitalizations receiving thrombolytics averaged over 2013 and 2014.

Etiology of readmission at 30 days	**Odd ratio (presented as cancer vs non-cancer)**	**p-value**	**Etiology of readmission at 90 days**	**Odd ratio (presented as cancer vs non-cancer)**	**p-value**
Overall readmission (9.5% in cancer vs 9.1% in non-cancer)	1.04 (0.78-1.40)	0.78	Overall readmission (17.2% in cancer vs 13.3% in non-cancer)	1.35 (1.06-1.73)	0.02
Ischemic Stroke	0.77 (0.41-1.43)	0.40	Ischemic Stroke	0.65 (0.39-1.08)	0.10
Hemorrhagic Stroke	1.62 (0.48-5.59)	0.44	Hemorrhagic Stroke	2.07 (0.79-5.43)	0.14
Bleeding	0.46 (0.07-3.40)	0.45	Bleeding	0.60 (0.18-2.01)	0.41
Infection	1.14 (0.58-2.23)	0.71	Infection	1.61 (0.99-2.61)	0.051
All Arrhythmias	0.39 (0.05-2.84)	0.35	All Arrhythmias*	-	
Atrial Fibrillation	0.57 (0.08-4.20)	0.58	Atrial Fibrillation*	-	
Congestive Heart Failure	1.73 (0.51-5.87)	0.38	Congestive Heart Failure	1.31 (0.55-3.13)	0.54
Hematologic	3.44 (1.29-9.15)	0.01	Hematologic	4.44 (2.15-9.15)	<0.0001
Respiratory	1.83 (0.44-7.68)	0.41	Respiratory	1.34 (0.40-4.38)	0.65
Gastrointestinal	0.62 (0.15-2.60)	0.51	Gastrointestinal	0.85 (027-2.69)	0.78
Genitourinary	0.30 (0.07-1.26)	0.10	Genitourinary	0.27 (0.08-0.85)	0.03

*0 % in cancer hence OR not calculated

Moreover, there was no difference in tPA utilization among cancer patients, based on anticancer therapy status (42.4 vs. 42.8 administrations per 1,000 AIS in non-anticancer therapy vs active cancer therapy; P = 0.82).

Table S4. Diagnosis codes to identify in-hospital complications.

Procedure	ICD-9 code
Intracranial hemorrhage	430.xx,431.xx,432.xx
Gastrointestinal bleeding	578.xx
All bleeding	Above codes, 729.92, 599.70, 998.1x, 459.0x, 285.1x

Supplemental References

1. Collaborators GBDLRoS, Feigin VL, Nguyen G, et al. Global, Regional, and Country-Specific Lifetime Risks of Stroke, 1990 and 2016. N Engl J Med 2018;379(25):2429-37.
2. Houchens RL, Ross DN, Elixhauser A, Jiang J. Nationwide Inpatient Sample Redesign: Final Report. Rockville, MD; 2014 [updated 2014; cited 2018 6/25]; Available from: https://www.hcup-us.ahrq.gov/reports/methods/2014-04.pdf.
3. Trend Weights for HCUP NIS Data. Rockville, MD; 2015 [updated 2015 5/12/15; cited 2018 6/25]; Available from: https://www.hcup-us.ahrq.gov/db/nation/nis/trendwghts.jsp.
4. Barrett ML. 2015 Healthcare Cost and Utilization Project (HCUP) National Inpatient Sample: Change in Structure and Data Elements Caused by Transition to ICD-10-CM/PCS. Online, Rockville, MD: U.S. Agency for Healthcare Research and Quality; 2017 [updated 2017 11/10/2017; cited 2018 6/25]; Available from: https://www.hcup-us.ahrq.gov/db/nation/nis/2015HCUPNationalInpatientSample.pdf.
5. Moore BJ, White S, Washington R, Coenen N, Elixhauser A. Identifying Increased Risk of Readmission and In-hospital Mortality Using Hospital Administrative Data: The AHRQ Elixhauser Comorbidity Index. Med Care 2017;55(7):698-705.
6. Bland JM, Altman DG. Transformations, means, and confidence intervals. BMJ 1996;312(7038):1079.
7. Gilbert BD, Horstman JM. Captain's LOG: Taking Command of SAS® Logarithm Functions. 2014 [updated 2014; cited 2018 6/25]; Available from: https://www.mwsug.org/proceedings/2014/RF/MWSUG-2014-RF06.pdf.
8. Cost-to-Charge Ratio Files. Rockville, MD; 2017 [updated 2017 11/15/2017; cited 2018 6/25]; Available from: https://www.hcup-us.ahrq.gov/db/state/CCR_NIS_UserGuide_2001-2015.pdf.
9. Kwok CS, Martinez SC, Pancholy S, et al. Effect of Comorbidity On Unplanned Readmissions After Percutaneous Coronary Intervention (From The Nationwide Readmission Database). Sci Rep 2018;8(1):11156.
10. Navi BB, Reiner AS, Kamel H, et al. Risk of Arterial Thromboembolism in Patients With Cancer. J Am Coll Cardiol 2017;70(8):926-38.
11. Thigpen JL, Dillon C, Forster KB, et al. Validity of international classification of disease codes to identify ischemic stroke and intracranial hemorrhage among individuals with associated diagnosis of atrial fibrillation. Circ Cardiovasc Qual Outcomes 2015;8(1):8-14.

12. HCUP Elixhauser Comorbidity Software, Healthcare Cost and Utilization Project (HCUP). Agency for Healthcare Research and Quality, Rockville, MD; 2017 [updated 2017 6/12/2017; cited 2018 11/03]; Available from: ww.hcup-us.ahrq.gov/toolssoftware/comorbidity/comorbidity.jsp.
13. Overview of Disease Severity Measures Disseminated with the Nationwide Inpatient Sample (NIS) and Kids' Inpatient Database (KID). Rockville, MD; 2005 [updated 2005 12/09/05; cited 2018 6/25]; Available from: https://www.hcup-us.ahrq.gov/db/nation/nis/OverviewofSeveritySystems.pdf.
14. Houchens R, Ross D, Elixhauser A. Final Report on Calculating National Inpatient Sample (NIS) Variances for Data Years 2012 and Later. ONLINE; 2015 [updated 2015 5/19/16; cited 2018 6/25]; Available from: https://www.hcup-us.ahrq.gov/reports/methods/2015_09.jsp.
15. Houchens R, Elixhauser A. Final Report on Calculating Nationwide Inpatient Sample (NIS) Variances for Data Years 2011 and Earlier. ONLINE; 2015 [updated 2015 5/18/16; cited 2018 6/25]; Available from: https://www.hcup-us.ahrq.gov/reports/methods/2003_02.jsp.
16. Yoon F, Sheng M, Jiang HJ, Steiner CA, Barrett ML. Calculating Nationwide Readmissions Database (NRD) Variances. U.S. Agency for Healthcare Research and Quality.; 2017 [updated 2017; cited 2018 7/28]; Available from: : http://www.hcupus.ahrq.gov/reports/methods/methods.jsp.
17. Khera R, Angraal S, Couch T, et al. Adherence to Methodological Standards in Research Using the National Inpatient Sample. JAMA 2017;318(20):2011-8.
18. Khera R, Krumholz HM. With Great Power Comes Great Responsibility: Big Data Research From the National Inpatient Sample. Circ Cardiovasc Qual Outcomes 2017;10(7).
19. Navi BB, Singer S, Merkler AE, et al. Recurrent thromboembolic events after ischemic stroke in patients with cancer. Neurology 2014;83(1):26-33.
20. Parsons LS, editor. Performing a 1: N case-control match on propensity score. proceedings of the 29th Annual SAS users group international conference; 2004. SAS Institute.
21. VanderWeele TJ, Ding P. Sensitivity Analysis in Observational Research: Introducing the E-Value. Ann Intern Med 2017;167(4):268-74.