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Rate of venous thromboembolism among surgical patients in Australian hospitals: A population-based study

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Rate of Venous Thromboembolism among Surgical Patients in Australian Hospitals: A Population-based Study

ABSTRACT

Background: Despite the burden of venous thromboembolism (VTE) among surgical patients on health systems in Australia, data on VTE incidence and its variation within Australia is lacking**.**

Objective: To explore VTE incidence and associated mortality rates, and their trends and variations across Australian acute public hospitals.

Design and Setting: A population-based study using all elective surgical patients in 82 acute public hospitals during 2002-2009 in New South Wales, Australia.

Participants: Patients who had elective surgery within two days of admission, aged between 18 – 90 years, and were not transferred to another acute care facility; 4,362,624 patients were included.

Outcome Measures: VTE incidents were identified by secondary diagnostic codes. Poisson mixed models were used to derive adjusted incidence rates and rate ratios (IRR) in presence of patient and hospital characteristics.

Results: Two per 1000 patients developed post-operative VTE. VTE increased by 28% (IRR=1.28, CI: 1.17-1.40) over the study period. Differences in the VTE rates, trends between hospital peer groups and between hospitals with the highest and those with the lowest rates were significant (between-hospital variation). Smaller hospitals, accommodated in two peer groups, had the lowest overall VTE rates (IRR=0.56:0.32-1.00; and IRR=0.32:0.18-0.55) and exhibited a greater increase (61% and 241% vs. 17%) over time and greater between-hospital variations compared to larger hospitals (IRR=9.90:7.16-13.67; and IRR=8.86:5.45-14.40 vs. IRR=4.46:4.40-4.97). Mortality among patients with post-operative VTE was 8% and remained stable over time (IRR=1.01:0.97-1.04). No differences in post-VTE death rates and trends were seen between hospital groups; however larger hospitals exhibited less between-hospital variations (IRR=1.99:1.43-2.77) compared to small hospitals (IRR=37.00:10.11-101.35). Hospitals performed differently in prevention versus treatment of post-operative VTE.

Conclusions: The incidence of VTE is increasing and there is large variation between- and within-hospital peer groups suggesting a varied compliance with VTE preventative strategies and the potential for targeted interventions and quality improvement opportunities.

ARTICLE SUMMARY

Article focus

- To evaluate rates and trends of post-operative VTE incidence and subsequent mortality within Australian hospitals
- To demonstrate and compare variations of VTE incidence and subsequent deaths between hospitals

Key messages

- Post-operative VTE incidence rate was two per 1000 patients. It increased by 28% over the study period. Post-VTE mortality rate was 8% and remained stable over time.
- Smaller hospitals had lower VTE rates but exhibited a greater increase over time and greater between-hospital variations compared to larger hospitals. They also exhibited greater between-hospital variations in post-VTE death rates.

Strengths and limitations of this study

- This study benefited from a population-based design within the largest health jurisdiction in Australia.
- Employment of standardised and broadly-applied VTE measures facilitated local and international comparisons and benchmarking.
- Demonstration of trends and variations in VTE measures reflected effectiveness of systematic interventions and revealed opportunities for further improvement and actions at local and regional levels.
- This study was limited to VTE incidence among elective surgical patients. Analysis of all patient populations may provide addition insight.
- The obtained rates may have under-estimated due to possible coding discrepancies.

INTRODUCTION

Venous thromboembolism (VTE), comprised of deep-vein thrombosis (DVT) and pulmonary embolism (PE), can cause long-term comorbidities or death[1 2] and incur significant financial burden on healthcare systems.[3 4] It accounts for nearly 10% of all deaths in U.S. [5 6] and Australian hospitals,[7 8] and is amongst the top five most common causes of hospital-related deaths in both countries.[3 9] However, VTE is also the most common preventable cause of hospital deaths.[10-13] A significant decrease in VTE incidents has been reported where efficacious and cost-effective treatments (ie. pharmacological and mechanical prophylaxis) were used for both medical and surgical patients.[1 12 14-19] Accordingly, several evidence-based VTE prevention and treatment guidelines were developed[1 9 20] and related measures were adopted among quality of care indices for accreditation, quality improvement and benchmarking purposes.[21-23]

The Agency for Healthcare Research and Quality (AHRQ) listed post-operative VTE complications and subsequent death as a component of failure-to-rescue (FTR) among patient saftey indicators (PSI#12 and PSI#4-2 respectively), which are routinely being monitored and publically reported.[23 24] Reports showed that the post-operative VTE incidence rates have nearly halved in U.S. hospitals in recent years,[24 25] and post-VTE mortality rate declined by a third within a decade since the mid-90s.[26] These rate decreases may be, in part, due to the implementation of post-operative VTE prevention protocols,[27] however substantial variation in post-operative VTE incidence rate was also evident among U.S. hospitals.[25] Although patients case mix and surgery types may play a role in such differences,[6 28 29] the variation of VTE incidence among the same type of hospitals over time and within the group may reflect the success of quality improvement interventions and demonstrate the potential for further development.[30 31]

Few Australian studies have reported VTE incidence,[3 8 32] and the measures of VTE used in these studies varied making comparison difficult. Consequently, we employed the internationally-recognised AHRQ measures for post-operative VTE, and subsequent mortality, to explore the trend of the incidence rates and their variations among admitted surgical patients in acute public hospitals across New South Wales (NSW), Australia (2002-2009).

METHODS

Data source and study population

New South Wales is the largest health jurisdiction in Australia with approximately 497 healthcare facilities and a population of over seven million people. We used records from the NSW Admitted

Patient Data Collection (APDC) database, which includes all admitted patient services provided by NSW public and private healthcare facilities. The APDC includes information on patient demographics, medical conditions and procedures, hospital characteristics, and separations (discharges, transfers and deaths) from all public and private hospitals (as well as day procedure centres) in NSW. The medical records for each episode of care in the APDC were assigned with codes based on the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification (ICD-10-AM) 4th edition.[33] Of admissions at 497 healthcare facilities across NSW between 1st January 2002 to 31st December 2009, we included all 82 NSW acute public hospitals (9,221,128 admissions; 57.4%) in our study. Two children's hospitals and one other hospital (data was unavailable) were excluded We restricted our study to only elective surgical patients and applied the same AHRQ inclusion criteria[23] for patients who had elective surgery within two days of admission, aged between 18 – 90 years (inclusive), and were not transferred to another acute care facility (4,362,624 episodes (47.3%)). Ethical approval was obtained from the University of NSW Human Research Ethics Committee (LNR/11/CIPHS/64).

Measures and covariates

Patients who developed VTE were identified by secondary diagnostic codes (ICD-10-AM) translated from the AHRQ definition (ICD-9-CM) by Victorian Government Health Information.[34] We employed the term "post-operative VTE" from the Australian version of patient safety indicators (AusPSI)[35] instead of "peri-operative VTE" developed by AHRQ. In combination with discharge status, patients post-VTE outcomes were categorised as survival or death. VTE and related death rates were presented as incidences per 1000 admissions within each year between 2002 and 2009, inclusively.

Two sets of patient- and hospital-related covariates were considered. Patient demographic variables included age, gender, country of birth, marital status, patient socio-economic status, and principle diagnostic disease groups (the ten most common) within the study population. We utilised a postcode-level advantage and disadvantage index of Socio-Economic Indices for Areas (SEIFA) with the lower values indicating more disadvantaged areas.[36] SEIFA scores were categorised into four classes (1st quartile = most disadvantaged areas and 4th quartile = most advantaged areas). The disease groups were identified using principle diagnostic codes (ICD-10-AM) at admissions through the methodology develop by Quan et al..[37]

Hospital covariates included the local health district (metropolitan, rural and regional NSW) and peer group (A1: principal referral group, usually teaching hospitals; A3: ungrouped acute; B: major metropolitan and non-metropolitan; C1: district group 1; and, C2: district group 2). Hospital peer

groups contained similar type and sized hospitals, ranging from those treating more than 25,000 acute case-mix weighted separations per annum in principal referral groups through to treating 2,000+ (but less than 5,000) acute case-mix weighted separations per annum in district group 2.[38]

Statistical analysis

We employed Poisson mixed models to evaluate adjusted incidence rates and rate ratios for study outcomes after including all patients and hospital-related characteristics. A random intercept term was utilised to incorporate any clustering effect at hospital-level. To investigate the temporal behaviour of the outcomes, calendar years were entered into the model as indicator variables, with 2002 as the reference year. A model with the year as a continuous variable was also examined for linear trends. We derived hospital peer group trends using an interaction effect (year and hospital peer group) in a separate model. Adjusted incidence rates for specific years were derived by multiplying yearly-adjusted risk ratios to the crude risks observed in the reference year.

We initially examined the Elixhauser and the Charlson Index comorbidities based on the ICD-10 coding scheme,[37] however we did not include either of them in the models given recent reports that these indices may introduce misleading results possibly due to geographical variations and biases in the coding.[39-41] To study the variation of outcomes across hospitals within each hospital group, hospital-specific random intercept components were extracted from Poisson mixed models constructed for each hospital group, then ranked and categorised into five classes at 20% incremental quintiles. To obtain adjusted differences between those with the highest and those with the lowest VTE incidence, the adjusted classes were entered into a Poisson model including patient characteristics covariates. We used Pearson correlation to assess the association of hospital performances between VTE and post-VTE deaths, based on the hospital-specific random intercepts. All analyses were performed in R package version 3.0.0[42] and Stata™ 11.0.[43]

RESULT

Error! Reference source not found. summarised the study population by outcomes across hospital and patient characteristics and related statistics. Of the 4,223,317 (45.8% of all admissions with no missing information) elective surgical admissions during 2002-2009, 8,451 patients developed either DVT or PE after surgery, resulting in an incidence rate of 2 per 1000 surgical patients. Among them, 671 died prior to discharge (8%); 79.6 per 1000 patients with post-operative VTE. Compared to females, males tended to have a lower risk of post-operative VTE (IRR=0.87); however, they were more likely to die (IRR=1.23) following a VTE. Older patients were exposed to higher risks of VTE and death after surgery. Married patients and those who were born in Asia and North Africa

experienced a lower risk of post-operative VTE compared to their counterparts but a similar risk of post-VTE death.

Patients admitted with malignancy and congestive heart failure had the highest VTE and hospital mortality rates. Higher socio-economic status (quartiles of SEIFA) of patients was associated with a lower risk of VTE. There was no difference in mortality for patients residing in advantaged and disadvantaged areas. Patients from principal referral hospitals were more likely to acquire VTE in comparison to the patients from district hospitals (IRR= 0.56 and 0.32 for group 1 and 2 hospitals respectively). No differences in outcomes were observed between metropolitan and non-metropolitan hospitals.

Post-operative VTE incidence rate significantly increased over the study period by 28%, from 1.77 per 1000 patients in 2002 to 2.20 in 2009 (Figure 1). Despite some fluctuation, all hospital peer groups exhibited similar increasing trends in post-operative VTE incidence over the study period after adjustment for patient demographics (Figure 2), ranging from 17% (2.55 vs. 2.17) in principal referral hospitals to 241% (1.23 vs. 0.36) in district group 2. Post-VTE mortality fluctuated between 68 to 97 cases per 1000 patients over the study period with no significant change after adjusting for confounders overall (Figure 1) and at hospital peer group level (Figure 2). Mortality tended to be stable across hospital peer groups as between-group variation of mortality reduced over the study period.

The incidence rate ratios between those hospitals with the lowest, and those with the highest rate, was larger in VTE related mortality than in VTE and varied across hospital peer group (**Error! Reference source not found.**). For VTE, the difference in rate is less than five-fold in the principal referral and ungrouped acute hospital peer groups but at least eight-fold in other peer groups. Similarly, the difference in rate is larger in district group 1 (IRR=37) compared to principal referral (IRR=2) and major metropolitan/non-metropolitan hospitals (IRR=15) for VTE related deaths. The significant negative correlation (-0.62) for principal referral hospitals implied that hospitals with the highest post-operative VTE rate tended to have a lower rate of subsequent death. In contrast, within district group 2 (0.40), hospitals with higher VTE rates tended to also have the highest post-VTE death rates. There were no such associations within other peer groups.

Table 1. Incidence rates (IR) and adjusted incidence rate ratios (IRR) of surgical patients who developed VTE and died, stratified by patient and hospital characteristics.

Characteristics	Surgical patients n (%)	VTE			VTE associated death		
		Frequency (%)	IR	IRR (95% CI)	Frequency (%)	IR	IRR (95% CI)
Sex							
Female	2280384 (54.00)	4626 (54.74)	2.03	1.00	330 (49.03)	71.34	1.00
Male	1942933 (46.00)	3825 (45.26)	1.97	0.87 (0.83-0.91) **	343 (50.97)	89.67	1.23 (1.05-1.44) **
Age							
>=18yr & <35yr	738382 (17.48)	487 (5.76)	0.66	0.18 (0.17-0.20) **	11 (1.63)	22.59	0.21 (0.11-0.39) **
>=35yr & <55yr	1013921 (24.01)	1308 (15.48)	1.29	0.38 (0.36-0.41) **	82 (12.18)	62.69	0.59 (0.46-0.76) **
>=55yr & <75yr	1595024 (37.77)	3538 (41.86)	2.22	0.67 (0.64-0.71) **	290 (43.09)	81.97	0.81 (0.68-0.96) *
>=75yr & <90	875990 (20.74)	3118 (36.90)	3.56	1.00	290 (43.09)	93.01	1.00
Marital status							
Married	2548508 (60.34)	4667 (55.22)	1.83	1.00	381 (56.61)	81.64	1.00
Single	1674809 (39.66)	3784 (44.78)	2.26	1.16 (1.11-1.21) **	292 (43.39)	77.17	0.99 (0.84-1.16)
Country of birth							
Australia and New Zealand	2839135 (67.23)	5858 (69.32)	2.06	1.00	479 (71.17)	81.77	1.00
UK, US & Canada	239088 (5.66)	645 (7.63)	2.70	1.09 (1.00-1.18)	53 (7.88)	82.17	0.95 (0.71-1.27)
Non-English Europe	447239 (10.59)	1046 (12.38)	2.34	0.73 (0.68-0.79) **	80 (11.89)	76.48	0.88 (0.68-1.12)
North Africa	130938 (3.10)	139 (1.64)	1.06	0.45 (0.38-0.53) **	9 (1.34)	64.75	0.88 (0.45-1.71)
Asia	179725 (4.26)	193 (2.28)	1.07	0.44 (0.38-0.51) **	16 (2.38)	82.90	0.83 (0.46-1.50)
Others	387192 (9.17)	570 (6.74)	1.47	0.57 (0.52-0.62) **	36 (5.35)	63.16	0.88 (0.62-1.24)
Major principle diagnostic diseases†							
Cardiac arrhythmias	25953 (0.61)	75 (0.89)	2.89	-	2 (0.30)	26.67	-
Chronic pulmonary disease	11558 (0.27)	69 (0.82)	5.97	-	6 (0.89)	86.96	-
Coagulopathy	3908 (0.09)	37 (0.44)	9.47	-	2 (0.30)	54.05	-
Congestive heart failure	6765 (0.16)	85 (1.01)	12.56	-	17 (2.53)	200.00	-
Diabetes with chronic complication	33541 (0.79)	79 (0.93)	2.36	-	11 (1.63)	139.24	-
Malignancy including lymphoma & leukaemia	150962 (3.57)	1070 (12.66)	7.09	-	182 (27.04)	170.09	-
Metastatic solid tumour	19699 (0.47)	291 (3.44)	14.77	-	67 (9.96)	230.24	-
Peripheral vascular disease	15993 (0.38)	141 (1.67)	8.82	-	10 (1.49)	70.92	-
Renal failure	1385753 (32.81)	42 (0.50)	0.03	-	1 (0.15)	23.81	-
Rheumatoid arthritis/collagen vascular disease	10748 (0.25)	40 (0.47)	3.72	-	1 (0.15)	25.00	-
Year							
2002	431184 (10.21)	763 (9.03)	1.77	1.00	65 (9.66)	85.19	1.00

2003	438058 (10.37)	780 (9.23)	1.78	1.01 (0.92-1.12)		53 (7.88)	67.95	0.84 (0.58-1.21)
2004	462451 (10.95)	878 (10.39)	1.90	1.09 (0.99-1.20)		65 (9.66)	74.03	0.83 (0.59-1.18)
2005	508097 (12.03)	1038 (12.28)	2.04	1.18 (1.08-1.30)	**	75 (11.14)	72.25	0.78 (0.56-1.09)
2006	550688 (13.04)	1062 (12.57)	1.93	1.12 (1.02-1.23)	*	103 (15.30)	96.99	1.01 (0.74-1.39)
2007	591973 (14.02)	1223 (14.47)	2.07	1.22 (1.11-1.33)	**	87 (12.93)	71.14	0.75 (0.54-1.04)
2008	607631 (14.39)	1313 (15.54)	2.16	1.26 (1.15-1.38)	**	112 (16.64)	85.30	0.94 (0.69-1.28)
2009	633235 (14.99)	1394 (16.50)	2.20	1.28 (1.17-1.40)	**	113 (16.79)	81.06	0.87 (0.63-1.18)
Year-linear trend	-	-	-	1.03 (1.02-1.04)	**	-	-	1.01 (0.97-1.04)
Quartiles of SEIFA								
1st quartile (most disadvantaged)	1089833 (25.81)	2308 (27.31)	2.12	1.00		187 (27.79)	81.02	1.00
2nd quartile	1084727 (25.68)	1981 (23.44)	1.83	0.88 (0.82-0.93)	**	169 (25.11)	85.31	0.95 (0.76-1.18)
3rd quartile	1074283 (25.44)	2088 (24.71)	1.94	0.75 (0.71-0.80)	**	175 (26.00)	83.81	1.01 (0.81-1.26)
4th quartile (most advantaged)	974474 (23.07)	2074 (24.54)	2.13	0.66 (0.62-0.71)	**	142 (21.10)	68.47	0.98 (0.77-1.26)
Peer hospital groups								
Principal referral	2269392 (53.73)	5141 (60.83)	2.27	1.00		381 (56.61)	74.11	1.00
Ungrouped acute	133465 (3.16)	380 (4.50)	2.85	1.05 (0.44-2.50)		43 (6.39)	113.16	0.93 (0.32-2.70)
Major metro- & non-metropolitan	1140036 (26.99)	2125 (25.14)	1.86	0.85 (0.52-1.39)		183 (27.19)	86.12	0.88 (0.51-1.52)
District group 1	346910 (8.21)	484 (5.73)	1.40	0.56 (0.32-1.00)	*	42 (6.24)	86.78	0.94 (0.47-1.89)
District group 2	333514 (7.90)	321 (3.80)	0.96	0.32 (0.18-0.55)	**	24 (3.57)	74.77	0.77 (0.37-1.61)
Local health district								
Metropolitan	2720690 (64.42)	5882 (69.60)	2.16	1.00		430 (63.89)	73.10	1.00
Rural & Regional NSW	1502627 (35.58)	2569 (30.40)	1.71	0.70 (0.48-1.02)		243 (36.11)	94.59	1.32 (0.82-2.13)
Total	4223317	8451	2.00	-		673	79.64	-

139,307 (3.2%) cases were excluded due to missing or unknown items.
Incidence rates (IR) are crude and reported per 1000 patients.
Risk ratios (RR) and related confident intervals (CI) were obtained using a Poisson mixed model.
† No RR is reported since this characteristic has not been included in the Poisson mixed model.
* Significant at 5%; ** significant at 1%.

Table 2. Incidence rates (IR), adjusted incidence rate ratios (IRR) and association of outcomes between the best and worst performers (top and bottom 20% quintiles) within hospital peer groups

Hospital peer group	Hospital n	VTE				Post-VTE death				Correlation coefficient (95% CI)	
		Lowest (IR)	Highest (IR)	IRR (95% CI)		Lowest (IR)	Highest (IR)	IRR (95% CI)			
Principal referral	14	1.24	4.97	4.46 (4.00-4.97)	**	38.60	124.17	1.99 (1.43-2.77)	**	-0.62 (-0.86,-0.13)	*
Ungrouped acute† §	3	0.65	7.30	9.91 (6.53-15.02)	**	0.00	142.36	-		-	
Major metro- & non-metropolitan	22	0.89	2.87	4.56 (3.92-5.31)	**	16.80	148.81	15.08 (6.27-36.23)	**	0.14 (-0.30,0.53)	
District group 1	13	0.42	3.71	9.90 (7.16-13.67)	**	13.88	242.71	37.00 (10.11-101.35)	**	-0.36 (-0.76,0.24)	
District group 2†	30	0.22	2.15	8.86 (5.45-14.40)	**	0.00	109.19	-		0.40 (0.03,0.67)	*

Incidence rates (IR) are crude and reported per 1000 patients.
Risk ratios (RR) and related confident intervals (CI) were obtained using a Poisson model and adjusted for patient characteristics. Those hospitals with the lowest rate were set as the reference level.
† No RR is reported for Post-VTE death due to zero incidences in the reference level.
§ No correlation coefficient is reported due to small number of hospitals within this group.
* Significant at 5%; ** significant at 1%.

DISCUSSION

In this population-based study, of elective surgical patients, from all NSW acute public hospitals, over an 8 year period, we found that the incidence of VTE to be two of 1000 elective surgical admissions, and VTE associated mortality to be 8%. The adjusted incidence of VTE increased significantly over the study period (28%), with no change in mortality. There were significant differences in incidence of VTE between hospital peer groups and between hospitals with the lowest and those with the highest rate. Principal referral hospitals exhibited a higher overall incidence, but lower intragroup variation compared to other peer groups. Principal referral hospitals with a higher incidence of VTE also tended to have a lower VTE-related mortality.

The incidence of post-operative VTE in NSW hospitals was less than half that of. U.S. hospitals within a similar period (4.5 or more per 1000 patients in 2010 and prior),[25 44] but with a similar VTE associated mortality (83 vs. 79 per 1000 patients). [25] Based upon our findings, VTE incidence and associated mortality contributes to approximately 15% and 8% of overall failure-to-rescue (FTR)-related incidence and mortality (13.8 and 140 per 1000 patients, respectively).[45] Despite the fact that our study and the U.S. study used the identical measure defined by AHRQ,[23] the discrepancies and coding practices between the U.S. (ICD-9-CM) and Australia (ICD-10-AM) may, in part, have contributed to the difference. It was shown that accuracy of VTE coding can be improved by the adoption of extended codes developed in the revised ICD-9-CM. [46]

In a recent Organization for Economic and Co-Operation and Development (OECD) report, Australian-wide incidence were 0.97 and 1.26 per 1000 patients in 2009 and 2012 respectively, placing Australia among three nations (Australia, Slovenia and the U.S.) with the highest incidence of approximately one per a thousand surgical patients or more within the last decade.[47] Our observed rate for NSW hospitals was nearly double that of the OCED provided Australian rates, possibly due to the fact that we studied only elective surgical patients from acute public hospitals. Such cross-nations reports provide a platform for health service comparisons and the study of longitudinal variations. However, internal and external comparability of OCED results may be affected by the heterogeneity and biases of the different nation's coding systems.

Despite continued poor compliance with VTE prevention guidelines and VTE preventative measures,[48-51] post-operative VTE incidence in U.S. hospitals almost halved between 2007-2011.[24 44] In Australia, given the overt gap between evidence and practice of VTE prevention protocols,[52 53] the National Institute of Clinical Studies (NICS) launched a VTE prevention program in 85 public and private hospitals across Australia between 2005-2008 which resulted in

increased awareness of and adherence with VTE prevention guidelines.[2 54] However, we found an increasing trend in NSW post-operative VTE incidence rate within 2002-2009, with an approximate 3% annual increase and total increase of 28%, mostly contributed by the higher incidence in the smaller hospital peer groups (241%) compared to the large teaching hospital group (17%). The reason for this increase is unclear.

Our finding of a higher incidence of VTE and VTE associated mortality with increasing age is similar that observed by others.[29 55-57] Ageing previously accepted as a major contributing factor to the increasing trends in VTE rates for admitted patients in Australian hospitals.[3] However, despite that we have taken into account patient demographic characteristics including age and demonstrated an adjusted increasing trend for surgical patients, other factors such as patient mix and surgery type may also contribute to our observed trend. For example, the increase in major surgeries such as hip (39%) and knee (72%) replacement procedures with the highest post-operative VTE risk between 2002 and 2010 in Australia[1 58 59] are likely to have contributed to the upward trend in VTE rates. More research is required to examine the effect of these factors. In particular, comorbidity-specific analysis at hospital level is encouraged to minimise potential biases reported elsewhere.[39-41]

Although other studies suggest gender may not be a significant risk factor for VTE,[28 29 60] we found males were less likely to develop VTE complications, but more likely to subsequently die. We did not separately explore DVT and PE incidence and associated deaths between genders; but our higher mortality risk for males can be explained by the estimated higher odds of PE (vs. DVT which has a lower risk of death[29 60] for males compared to females (1.87 vs. 1.02 respectively) in Australian hospitals during our study period.[3]

Variation in the application of VTE prevention guidelines and other quality initiatives may have contributed to the differences in outcomes amongst the hospitals in our study. Smaller, district 1 and 2 peer groups hospitals, had a significantly lower VTE incidence rate compared to larger hospitals in NSW. This was in contrast with other studies which showed that larger hospitals have a lower mortality following major procedures, such as orthopaedic surgeries[61 62] and post-operative complications such as VTE.[63] A possible explanation for this discrepancy is that principal referral hospitals undertook higher risk patients and surgical complexity than the smaller district hospitals. Geographical variations in coding,[39-41] underreporting of VTE due to mis-coding to a more general cardiovascular item,[3 64] and high diagnosis likelihood of high-risk but asymptomatic post-operative patients[65] may also have contributed to elevated VTE rates in major hospitals. We did not observe differences between NSW hospital peer groups for VTE mortality, nor did other studies for

FTR rates.[45] However, we did observe greater variation in VTE mortality within peer groups comprising smaller sized hospitals in comparison to larger principal referral hospitals.

Our study showed a significant performance difference between hospitals, within each hospital peer group, with the highest and those with the lowest VTE incidence and associated mortality. Similarly, the association between the two outcomes also varied across groups. Smaller hospitals (district groups 1 and 2) exhibited larger differences in both outcomes, suggesting a greater variability of patient care practice and outcomes amongst this group of hospitals and the greater potential for intervention aimed at VTE prevention and treatment for this group. We also noted a positive association between VTE incidence and VTE mortality amongst smaller size hospital groups. In contrast, larger NSW hospitals had a higher VTE incidence but lower VTE associated mortality, suggests that there may be a volume-outcome relationship or a greater adherence to evidence-based prevention and treatment guidelines that may explain this better VTE associated mortality. Interestingly, if the higher incidence of VTE alone was used as a measure of failure-to-prevent, these hospitals may be considered to have performed poorly overall, despite the better VTE associated mortality. Conversely, if the higher incidence rates of VTE were largely due to patient selection and case-mix, these hospitals could be considered as better quality hospitals having a lower failure-to-rescue rate with better treatment outcomes. Further investigation into the factors that may explain these differences and the ideal reporting measures is warranted.

Our study raised several important policy implications. Firstly, despite the fact that national and state agencies had developed evidence-based guidelines, such as the Clinical Excellence Commission of NSW "Medication Safety",[66] in which VTE prevention practices were promoted and related incidents evaluated, the increasing incidence of VTE and unchanged VTE mortality question the effectiveness of current national policy and local programs in reducing VTE incidence and mortality. Secondly, the development of systematic local program based on relevant international experience in successfully reducing VTE rate and its related mortality needs urgent policy action. Thirdly, the large variability of VTE rate and its related mortality between and within different hospital peer groups suggests that there is room for improvement in both the prevention and treatment of VTE and that VTE still remains a preventable complication. Lastly, as an important indicator of the quality of care, the level of standardised reporting of VTE in Australia should be explored.

The strengths of our study are that it is the first population-based observational study across all acute public hospitals within the one (i.e. NSW) health region. We used a standardised measure and presented both incidence rates of VTE and VTE associated mortality, thus enabling to differentiate between the two outcome measures and allow for international comparisons. Limitations of our study

include that we specifically studied only elective surgical patients according to AHRQ definitions; whereas the analyses of all patient populations may provide addition insight. Future research needs to provide more evidence on the whole inpatient population. We also may have under-reported our findings because of possible coding discrepancies. Nevertheless, this study reinforced the importance of developing measures for combating post-operative VTE, and the continual monitoring and public reporting VTE incidence and mortality.[2 67]

CONCLUSION

The significant increase in VTE incidence among surgical patients over an eight-year period, and persisting level of VTE associated mortality, highlights the need for urgent policy interventions. The significant variation for both outcomes between, and within, different hospital peer groups suggests room for improvement in both the prevention and treatment of VTE. Routine measurement and disclosure of both VTE incidence and associated mortality can provide policy-makers, clinicians and researchers with opportunities to monitor and adjust for performance.

CONTRIBUTORS

Conceived and designed the study: HA, JC, AF, and KH. Prepared the data and performed the analyses: HA, JC, and LO. Wrote the paper: HA, JC, SH, AF, and KH.

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COMPETING INTERESTS

Authors had no conflict of interest.

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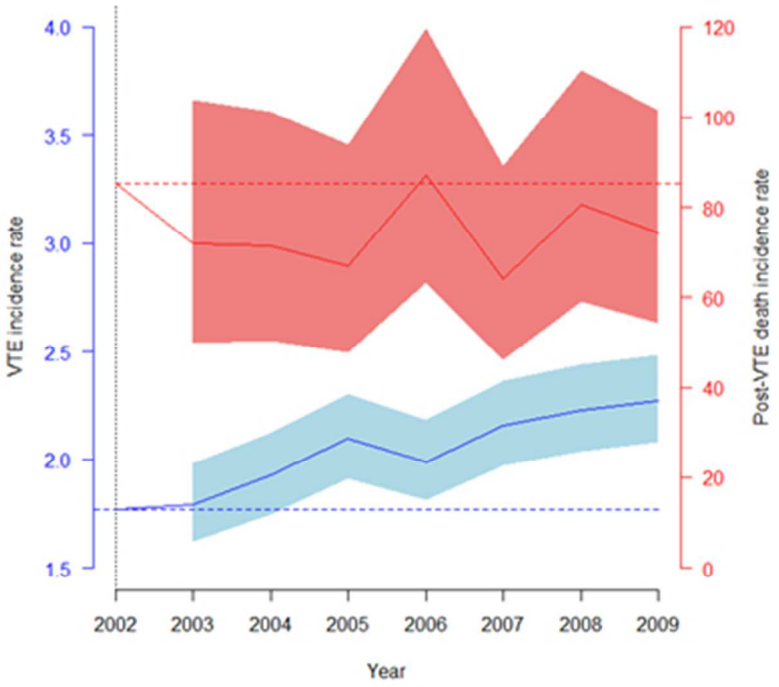
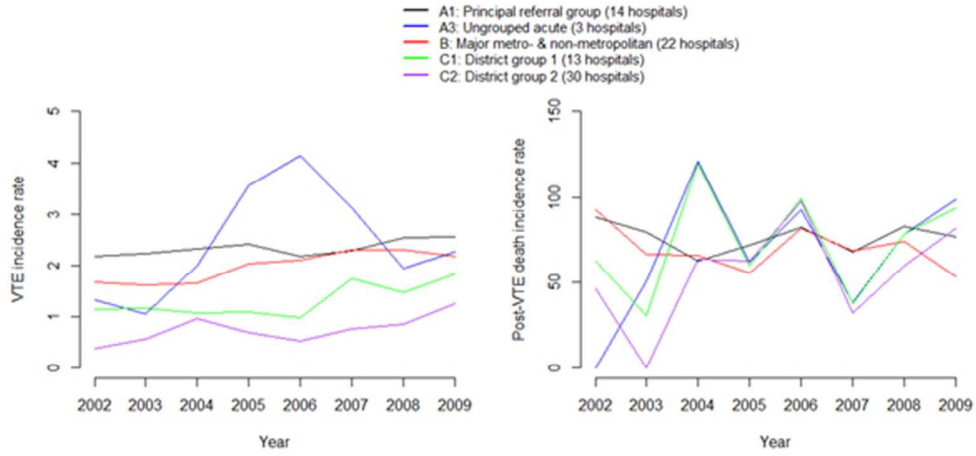
FIGURE LEGENDS

Figure 1. Adjusted trends of post-operative VTE and post-VTE death incidence rates over the study period. Rates were estimated by multiplying incidence rate ratio (obtained from the Poisson mix model) and crude risk at the reference year (2002).

Figure 2. Hospital peer group-specific adjusted trends of post-operative VTE (left panel) and post-VTE death (right panel) incidence rates over the study period. Rates were estimated by multiplying incidence rate ratio (obtained from the Poisson mix model including an interaction term for "hospital peer group × year") and crude risk of the reference hospital group (Principal referral) at the reference year (2002).



Adjusted trends of post-operative VTE and post-VTE death incidence rates over the study period. Rates were estimated by multiplying incidence rate ratio (obtained from the Poisson mix model) and crude risk at the reference year (2002).
105x90mm (96 x 96 DPI)



Hospital peer group-specific adjusted trends of post-operative VTE (left panel) and post-VTE death (right panel) incidence rates over the study period. Rates were estimated by multiplying incidence rate ratio (obtained from the Poisson mix model including an interaction term for "hospital peer group × year") and crude risk of the reference hospital group (Principal referral) at the reference year (2002).

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any pre-specified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5-6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	5
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-6
Bias	9	Describe any efforts to address potential sources of bias	6
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5-6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	6
		(*c*) Explain how missing data were addressed	6 , 8-Table 1
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	NA

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	6 (partly)
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8-Table 1
		(b) Indicate number of participants with missing data for each variable of interest	NA
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	NA
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	NA
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	NA
		Cross-sectional study—Report numbers of outcome events or summary measures	8-Table 1
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6-10(Tables 1 & T)
		(*b*) Report category boundaries when continuous variables were categorized	5, 8-10(Tables 1 & T)
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7, Figure 2
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11, 12 , 14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11-14
Generalisability	21	Discuss the generalisability (external validity) of the study results	11, 12, 14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Rate of venous thromboembolism among surgical patients in Australian hospitals: A large retrospective cohort study

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Title: Rate of venous thromboembolism among surgical patients in Australian hospitals: A large retrospective cohort study

Running title: Post-operative venous thromboembolism in Australia

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Rate of Venous Thromboembolism among Surgical Patients in Australian Hospitals: A Large Retrospective Cohort Study

ABSTRACT

Objectives: Despite the burden of venous thromboembolism (VTE) among surgical patients on health systems in Australia, data on VTE incidence and its variation within Australia is lacking. We aim to explore VTE incidence and associated mortality rates, and their trends and variations across Australian acute public hospitals.

Setting: A large retrospective cohort study using all elective surgical patients in 82 acute public hospitals during 2002-2009 in New South Wales, Australia.

Participants: Patients who had elective surgery within two days of admission, aged between 18 – 90 years, and were not transferred to another acute care facility; 4,362,624 patients were included.

Outcome Measures: VTE incidents were identified by secondary diagnostic codes. Poisson mixed models were used to derive adjusted incidence rates and rate ratios (IRR) in presence of patient and hospital characteristics.

Results: Two per 1000 patients developed post-operative VTE. VTE increased by 30% (IRR=1.30, CI: 1.19-1.42) over the study period. Differences in the VTE rates, trends between hospital peer groups and between hospitals with the highest and those with the lowest rates were significant (between-hospital variation). Smaller hospitals, accommodated in two peer groups, had the lowest overall VTE rates (IRR=0.56:0.33-0.95; IRR=0.37:0.23-0.61) and exhibited a greater increase (64% and 237% vs. 19%) over time and greater between-hospital variations compared to larger hospitals (IRR=8.64:6.23-11.98; IRR=8.92:5.49-14.49 vs. IRR=3.70:3.32-4.12). Mortality among patients with post-operative VTE was 8% and remained stable over time (IRR=0.98:0.95-1.02). No differences in post-VTE death rates and trends were seen between hospital groups; however larger hospitals exhibited less between-hospital variations (IRR=1.78:1.30-2.44) compared to small hospitals (IRR>23). Hospitals performed differently in prevention versus treatment of post-operative VTE.

Conclusions: The incidence of VTE is increasing and there is large variation between- and within-hospital peer groups suggesting a varied compliance with VTE preventative strategies and the potential for targeted interventions and quality improvement opportunities.

ARTICLE SUMMARY

Article focus

- To evaluate rates and trends of post-operative VTE incidence and subsequent mortality within Australian hospitals
- To demonstrate and compare variations of VTE incidence and subsequent deaths between hospitals

Key messages

- Post-operative VTE incidence rate was two per 1000 patients. It increased by 28% over the study period. Post-VTE mortality rate was 8% and remained stable over time.
- Smaller hospitals had lower VTE rates but exhibited a greater increase over time and greater between-hospital variations compared to larger hospitals. They also exhibited greater between-hospital variations in post-VTE death rates.

Strengths and limitations of this study

- This study benefited from a large cohort design within the largest health jurisdiction in Australia.
- Employment of standardised and broadly-applied VTE measures facilitated local and international comparisons and benchmarking.
- Demonstration of trends and variations in VTE measures reflected effectiveness of systematic interventions and revealed opportunities for further improvement and actions at local and regional levels.
- This study was limited to VTE incidence among elective surgical patients. Analysis of all patient populations may provide addition insight.
- The obtained rates may have under-estimated due to possible coding discrepancies.

INTRODUCTION

Venous thromboembolism (VTE), comprised of deep-vein thrombosis (DVT) and pulmonary embolism (PE), can cause long-term comorbidities or death[1 2] and incur significant financial burden on healthcare systems.[3 4] It accounts for nearly 10% of all deaths in U.S. [5 6] and Australian hospitals,[7 8] and is amongst the top five most common causes of hospital-related deaths in both countries.[3 9] However, VTE is also the most common preventable cause of hospital deaths.[10-13] A significant decrease in VTE incidents has been reported where efficacious and cost-effective treatments (ie. pharmacological and mechanical prophylaxis) were used for both medical and surgical patients.[1 12 14-19] Accordingly, several evidence-based VTE prevention and treatment guidelines were developed[1 9 20] and related measures were adopted among quality of care indices for accreditation, quality improvement and benchmarking purposes.[21-23]

The Agency for Healthcare Research and Quality (AHRQ) listed post-operative VTE complications and subsequent death as a component of failure-to-rescue (FTR) among patient saftey indicators (PSI#12 and PSI#4-2 respectively), which are routinely being monitored and publically reported.[23 24] Reports showed that the post-operative VTE incidence rates have nearly halved in U.S. hospitals in recent years,[24 25] and post-VTE mortality rate declined by a third within a decade since the mid-90s.[26] These rate decreases may be, in part, due to the implementation of post-operative VTE prevention protocols,[27] however substantial variation in post-operative VTE incidence rate was also evident among U.S. hospitals.[25] Although patients case mix and surgery types may play a role in such differences,[6 28 29] the variation of VTE incidence among the same type of hospitals over time and within the group may reflect the success of quality improvement interventions and demonstrate the potential for further development.[30 31]

Few Australian studies have reported VTE incidence,[3 8 32] and the measures of VTE used in these studies varied making comparison difficult. Consequently, we employed the internationally-recognised AHRQ measures for post-operative VTE, and subsequent mortality, to explore the trend of the incidence rates and their variations among admitted surgical patients in acute public hospitals across New South Wales (NSW), Australia (2002-2009).

METHODS

Data source and study population

New South Wales is the largest health jurisdiction in Australia with approximately 497 healthcare facilities and a population of over seven million people. We used records from the NSW Admitted

Patient Data Collection (APDC) database, which includes all admitted patient services provided by NSW public and private healthcare facilities. The APDC includes information on patient demographics, medical conditions and procedures, hospital characteristics, and separations (discharges, transfers and deaths) from all public and private hospitals (as well as day procedure centres) in NSW. The medical records for each episode of care in the APDC were assigned with codes based on the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification (ICD-10-AM) 4th edition.[33] Of admissions at 497 healthcare facilities across NSW between 1st January 2002 to 31st December 2009, we included all 82 NSW acute public hospitals (9,221,128 admissions; 57.4%) in our study. Two children's hospitals and one other hospital (data was unavailable) were excluded We restricted our study to only elective surgical patients and applied the same AHRQ inclusion criteria[23] for patients who had elective surgery within two days of admission, aged between 18 – 90 years (inclusive), and were not transferred to another acute care facility (4,362,624 episodes (47.3%)). Ethical approval was obtained from the University of NSW Human Research Ethics Committee (LNR/11/CIPHS/64).

Measures and covariates

Patients who developed VTE were identified by secondary diagnostic codes (ICD-10-AM) translated from the AHRQ definition (ICD-9-CM) by Victorian Government Health Information.[34] We employed the term "post-operative VTE" from the Australian version of patient safety indicators (AusPSI)[35] instead of "peri-operative VTE" developed by AHRQ. In combination with discharge status, patients post-VTE outcomes were categorised as survival or death. VTE and related death rates were presented as incidences per 1000 admissions within each year between 2002 and 2009, inclusively.

Two sets of patient- and hospital-related covariates were considered. Patient demographic variables included age, gender, country of birth, marital status, patient socio-economic status, and principle diagnostic disease groups (the ten most common) within the study population. We utilised a postcode-level advantage and disadvantage index of Socio-Economic Indices for Areas (SEIFA) with the lower values indicating more disadvantaged areas.[36] SEIFA scores were categorised into four classes (1st quartile = most disadvantaged areas and 4th quartile = most advantaged areas). The disease groups were identified using principle diagnostic codes (ICD-10-AM) at admissions through the methodology develop by Quan et al..[37] Using relevant procedure codes from ICD-10-AM (Appendix 1), we defined six major surgical procedures including coronary-artery bypass graft (CABG), abdominal aortic aneurysm (AAA) repair, total hip replacement, total knee replacement, cholecystectomy, and other surgical procedures.

Hospital covariates included the local health district (metropolitan, rural and regional NSW) and peer group (A1: principal referral group, usually teaching hospitals; A3: ungrouped acute; B: major metropolitan and non-metropolitan; C1: district group 1; and, C2: district group 2). Hospital peer groups contained similar type and sized hospitals, ranging from those treating more than 25,000 acute case-mix weighted separations per annum in principal referral groups through to treating 2,000^{+} (but less than 5,000) acute case-mix weighted separations per annum in district group 2.[38]

Statistical analysis

We employed Poisson mixed models to evaluate adjusted incidence rates and rate ratios for study outcomes after including all patients and hospital-related characteristics. A random intercept term was utilised to incorporate any clustering effect at hospital-level. To investigate the temporal behaviour of the outcomes, calendar years were entered into the model as indicator variables, with 2002 as the reference year. A model with the year as a continuous variable was also examined for linear trends. We derived hospital peer group and surgery type trends using interaction effects (year and hospital peer group; year and surgery type) in separate models. Adjusted incidence rates for specific years were derived by multiplying yearly-adjusted risk ratios to the crude risks observed in the reference year.

We initially examined the Elixhauser and the Charlson Index comorbidities based on the ICD-10 coding scheme,[37] however we did not include either of them in the models given an unexpected drop in the comorbidity index among our study population in recent years (Appendix 2) and also recent reports that these indices may introduce misleading results possibly due to geographical variations and biases in the coding.[39-41] To study the variation of outcomes across hospitals within each hospital group, hospital-specific random intercept components were extracted from Poisson mixed models constructed for each hospital group, then ranked and categorised into five classes at 20% incremental quintiles. To obtain adjusted differences between those with the highest and those with the lowest VTE incidence, the adjusted classes were entered into a Poisson model including patient characteristics covariates. We used Pearson correlation to assess the association of hospital performances between VTE and post-VTE deaths, based on the hospital-specific random intercepts. All analyses were performed in R package version 3.0.0[42] and Stata^{TM} 11.0.[43]

RESULT

Error! Reference source not found. summarised the study population by outcomes across hospital and patient characteristics and related statistics. Of the 4,223,317 (45.8% of all admissions with no missing information) elective surgical admissions during 2002-2009, 8,451 patients developed either

DVT or PE after surgery, resulting in an incidence rate of 2 per 1000 surgical patients. Among them, 673 died prior to discharge (8%); 79.6 per 1000 patients with post-operative VTE. Compared to females, males tended to have a lower risk of post-operative VTE (IRR=0.91); however, they were more likely to die (IRR=1.19) following a VTE. Older patients were exposed to higher risks of VTE and death after surgery. Married patients and those who were born in Europe (except the UK), Asia and North Africa experienced a lower risk of post-operative VTE compared to their counterparts but a similar risk of post-VTE death.

Patients admitted with malignancy and congestive heart failure had the highest VTE and hospital mortality rates. Patients who underwent total knee replacement, AAA repair and total hip replacement surgeries had higher risk of VTE, respectively; however, post-VTE mortality was lower among orthopaedic surgical patients compared to other procedures. Higher socio-economic status (quartiles of SEIFA) of patients was associated with a lower risk of VTE. There was no difference in mortality for patients residing in advantaged and disadvantaged areas. Patients from principal referral hospitals were more likely to acquire VTE in comparison to the patients from district hospitals (IRR= 0.56 and 0.37 for group 1 and 2 hospitals respectively). No differences in outcomes were observed between metropolitan and non-metropolitan hospitals.

Post-operative VTE incidence rate significantly increased over the study period by 30%, from 1.77 per 1000 patients in 2002 to 2.30 in 2009 (Figure 1). Despite some fluctuation, all hospital peer groups exhibited similar increasing trends in post-operative VTE incidence over the study period after adjustment for patient demographics (Figure 2), ranging from 19% (2.58 vs. 2.17) in principal referral hospitals to 237% (1.21 vs. 0.36) in district group 2. Surgery-specific VTE rates for the five procedures exhibited high fluctuations and insignificant trends, whereas the other surgery group showed a steady increasing trend of 38% (3.01 vs. 2.18) over the study period (Figure 3). Post-VTE mortality fluctuated between 68 to 97 cases per 1000 patients over the study period with no significant change after adjusting for confounders overall (Figure 1) and at hospital peer group level (Figure 2). Mortality tended to be stable across hospital peer groups as between-group variation of mortality reduced over the study period. No surgery-specific trend analysis was conducted due to small number of post-DVT deaths per annum.

The incidence rate ratios between those hospitals with the lowest, and those with the highest rate, was larger in VTE related mortality than in VTE and varied across hospital peer group (**Error! Reference source not found.**). For VTE, the difference in rate is less than four-fold in the principal referral and major peer groups (include large hospitals) but at least eight-fold in district peer groups (include small hospitals). Similarly, the difference in rate is larger in district group 1 and 2 (IRR=23 and 38)

compared to principal referral (IRR=1.7) and major metropolitan/non-metropolitan hospitals (IRR=15) for VTE related deaths. The close to significant negative correlation (-0.45, P-value=0.057) for principal referral hospitals implied that hospitals with the highest post-operative VTE rate tended to have a lower rate of subsequent death. In contrast, within district group 2 (0.41), hospitals with higher VTE rates tended to also have the highest post-VTE death rates. There were no such associations within other peer groups.

Table 1. Study population, incidence rates (IR) and adjusted incidence rate ratios (IRR) of surgical patients who developed VTE and died, stratified by patient and hospital characteristics.

Characteristics	Surgical patients n (%)	VTE			VTE associated death		
		Frequency (%)	IR	IRR (95% CI)	Frequency (%)	IR	IRR (95% CI)
Sex							
Female	2280384 (54.00)	4626 (54.74)	2.03	1.00	330 (49.03)	71.34	1.00
Male	1942933 (46.00)	3825 (45.26)	1.97	0.90 (0.86-0.94) **	343 (50.97)	89.67	1.19 (1.02-1.40) *
Age							
>=18yr & <35yr	738382 (17.48)	487 (5.76)	0.66	0.21 (0.19-0.23) **	11 (1.63)	22.59	0.20 (0.11-0.37) **
>=35yr & <55yr	1013921 (24.01)	1308 (15.48)	1.29	0.42 (0.40-0.45) **	82 (12.18)	62.69	0.58 (0.45-0.74) **
>=55yr & <75yr	1595024 (37.77)	3538 (41.86)	2.22	0.66 (0.63-0.70) **	290 (43.09)	81.97	0.85 (0.72-1.01)
>=75yr & <90	875990 (20.74)	3118 (36.90)	3.56	1.00	290 (43.09)	93.01	1.00
Marital status							
Married	2548508 (60.34)	4667 (55.22)	1.83	1.00	381 (56.61)	81.64	1.00
Single	1674809 (39.66)	3784 (44.78)	2.26	1.16 (1.11-1.21) **	292 (43.39)	77.17	1.01 (0.86-1.18)
Country of birth							
Australia and New Zealand	2839135 (67.23)	5858 (69.32)	2.06	1.00	479 (71.17)	81.77	1.00
UK, US & Canada	239088 (5.66)	645 (7.63)	2.70	1.06 (0.97-1.15)	53 (7.88)	82.17	0.95 (0.72-1.27)
Non-English Europe	447239 (10.59)	1046 (12.38)	2.34	0.74 (0.69-0.80) **	80 (11.89)	76.48	0.91 (0.71-1.16)
North Africa	130938 (3.10)	139 (1.64)	1.06	0.47 (0.40-0.56) **	9 (1.34)	64.75	0.87 (0.45-1.70)
Asia	179725 (4.26)	193 (2.28)	1.07	0.45 (0.39-0.52) **	16 (2.38)	82.90	1.09 (0.66-1.80)
Others	387192 (9.17)	570 (6.74)	1.47	0.58 (0.53-0.64) **	36 (5.35)	63.16	0.95 (0.67-1.35)
Major surgical procedure							
AAA repair	1744 (0.04)	26 (0.31)	14.91	1.00	6 (0.89)	230.77	1.00
CABG	10529 (0.25)	52 (0.62)	4.94	0.37 (0.23-0.60) **	7 (1.04)	134.62	0.69 (0.23-2.10)
Cholecystectomy	50145 (1.19)	42 (0.50)	0.84	0.09 (0.05-0.15) **	6 (0.89)	142.86	0.70 (0.22-2.22)
Total hip replacement	18771 (0.44)	207 (2.45)	11.03	0.74 (0.49-1.11)	4 (0.59)	19.32	0.12 (0.03-0.44) **
Total knee replacement	29428 (0.70)	798 (9.44)	27.12	1.76 (1.19-2.61) **	3 (0.45)	3.76	0.03 (0.01-0.11) **
Other	4112700 (97.38)	7326 (86.69)	1.78	0.17 (0.11-0.24) **	647 (96.14)	88.32	0.52 (0.23-1.19)
Major principle diagnostic diseases†							
Cardiac arrhythmias	25953 (0.61)	75 (0.89)	2.89	-	2 (0.30)	26.67	-
Chronic pulmonary disease	11558 (0.27)	69 (0.82)	5.97	-	6 (0.89)	86.96	-
Coagulopathy	3908 (0.09)	37 (0.44)	9.47	-	2 (0.30)	54.05	-
Congestive heart failure	6765 (0.16)	85 (1.01)	12.56	-	17 (2.53)	200.00	-
Diabetes with chronic complication	33541 (0.79)	79 (0.93)	2.36	-	11 (1.63)	139.24	-

Malignancy including lymphoma & leukaemia	150962 (3.57)	1070 (12.66)	7.09	-		182 (27.04)	170.09	-
Metastatic solid tumour	19699 (0.47)	291 (3.44)	14.77	-		67 (9.96)	230.24	-
Peripheral vascular disease	15993 (0.38)	141 (1.67)	8.82	-		10 (1.49)	70.92	-
Renal failure	1385753 (32.81)	42 (0.50)	0.03	-		1 (0.15)	23.81	-
Rheumatoid arthritis/collagen vascular disease	10748 (0.25)	40 (0.47)	3.72	-		1 (0.15)	25.00	-
Year								
2002	431184 (10.21)	763 (9.03)	1.77	1.00		65 (9.66)	85.19	1.00
2003	438058 (10.37)	780 (9.23)	1.78	1.01 (0.92-1.12)		53 (7.88)	67.95	0.85 (0.59-1.22)
2004	462451 (10.95)	878 (10.39)	1.90	1.09 (0.99-1.20)		65 (9.66)	74.03	0.82 (0.58-1.16)
2005	508097 (12.03)	1038 (12.28)	2.04	1.17 (1.07-1.29)	**	75 (11.14)	72.25	0.77 (0.55-1.08)
2006	550688 (13.04)	1062 (12.57)	1.93	1.11 (1.01-1.22)	*	103 (15.30)	96.99	1.02 (0.74-1.40)
2007	591973 (14.02)	1223 (14.47)	2.07	1.22 (1.12-1.34)	**	87 (12.93)	71.14	0.72 (0.52-1.01)
2008	607631 (14.39)	1313 (15.54)	2.16	1.27 (1.16-1.38)	**	112 (16.64)	85.30	0.90 (0.66-1.23)
2009	633235 (14.99)	1394 (16.50)	2.20	1.30 (1.19-1.42)	**	113 (16.79)	81.06	0.83 (0.60-1.13)
Year-linear trend	-	-	-	1.04 (1.03-1.05)	**	-	-	0.98 (0.95-1.02)
Quartiles of SEIFA								
1st quartile (most disadvantaged)	1089833 (25.81)	2308 (27.31)	2.12	1.00		187 (27.79)	81.02	1.00
2nd quartile	1084727 (25.68)	1981 (23.44)	1.83	0.88 (0.82-0.94)	**	169 (25.11)	85.31	0.96 (0.78-1.20)
3rd quartile	1074283 (25.44)	2088 (24.71)	1.94	0.76 (0.72-0.81)	**	175 (26.00)	83.81	1.04 (0.84-1.30)
4th quartile (most advantaged)	974474 (23.07)	2074 (24.54)	2.13	0.70 (0.65-0.75)	**	142 (21.10)	68.47	0.98 (0.77-1.26)
Peer hospital groups								
Principal referral	2269392 (53.73)	5141 (60.83)	2.27	1.00		381 (56.61)	74.11	1.00
Ungrouped acute	133465 (3.16)	380 (4.50)	2.85	1.20 (0.54-2.66)		43 (6.39)	113.16	0.94 (0.37-2.39)
Major metro- & non-metropolitan	1140036 (26.99)	2125 (25.14)	1.86	0.84 (0.54-1.31)		183 (27.19)	86.12	0.96 (0.60-1.55)
District group 1	346910 (8.21)	484 (5.73)	1.40	0.56 (0.33-0.95)	*	42 (6.24)	86.78	0.99 (0.54-1.83)
District group 2	333514 (7.90)	321 (3.80)	0.96	0.37 (0.23-0.61)	**	24 (3.57)	74.77	0.74 (0.38-1.44)
Local health district								
Metropolitan	2720690 (64.42)	5882 (69.60)	2.16	1.00		430 (63.89)	73.10	1.00
Rural & Regional NSW	1502627 (35.58)	2569 (30.40)	1.71	0.74 (0.52-1.05)		243 (36.11)	94.59	1.26 (0.82-1.92)
Total	4223317	8451	2.00	-		673	79.64	-

139,307 (3.2%) cases were excluded due to missing or unknown items.
Incidence rates (IR) are crude and reported per 1000 patients.
Risk ratios (RR) and related confident intervals (CI) were obtained using a Poisson mixed model.
CABG: Coronary Artery Bypass Graft; AAA repair: Abdominal Aortic Aneurysm repair.
† No RR is reported since this characteristic has not been included in the Poisson mixed model.
* Significant at 5%; ** significant at 1%.

Table 2. Incidence rates (IR), adjusted incidence rate ratios (IRR) and association of outcomes between the best and worst performers (top and bottom 20% quintiles) within hospital peer groups

Hospital peer group	Hospital n	VTE				Post-VTE death				Correlation coefficient (95% CI)	
		Lowest (IR)	Highest (IR)	IRR (95% CI)		Lowest (IR)	Highest (IR)	IRR (95% CI)			
Principal referral	17	1.24	4.00	3.70 (3.32-4.12)	**	43.58	131.12	1.78 (1.30-2.44)	**	-0.45 (-0.79, 0.01)	
Major metro- & non-metropolitan	22	1.00	2.99	3.85 (3.33-4.46)	**	16.80	162.30	15.48 (6.45-37.12)	**	0.15 (-0.28,0.54)	
District group 1	13	0.42	3.71	8.64 (6.23-11.98)	**	13.88	242.71	38.02 (10.25-140.94)	**	-0.37 (-0.76,0.22)	
District group 2	30	0.22	2.15	8.92 (5.49-14.49)	**	16.66	104.97	23.26 (2.94-183.50)	**	0.41 (0.05,0.68)	*

Incidence rates (IR) are crude and reported per 1000 patients.
Risk ratios (RR) and related confident intervals (CI) were obtained using a Poisson model and adjusted for patient characteristics. Those hospitals with the lowest rate were set as the reference level.
Ungrouped acute group was removed from analysis due to small number of hospitals within this group.
* Significant at 5%; ** significant at 1%.

DISCUSSION

In this large cohort study, of elective surgical patients, from all NSW acute public hospitals, over an 8 year period, we found that the incidence of VTE to be two of 1000 elective surgical admissions, and VTE associated mortality to be 8%. The adjusted incidence of VTE increased significantly over the study period (30%), with no change in mortality. There were significant differences in incidence of VTE between hospital peer groups and between hospitals with the lowest and those with the highest rate. Principal referral hospitals exhibited a higher overall incidence, but lower intragroup variation compared to other peer groups. Principal referral hospitals with a higher incidence of VTE also tended to have a lower VTE-related mortality.

The incidence of post-operative VTE in NSW hospitals was less than half that of. U.S. hospitals within a similar period (4.5 or more per 1000 patients in 2010 and prior),[25 44] but with a similar VTE associated mortality (83 vs. 79 per 1000 patients). [25] Based upon our findings, VTE incidence and associated mortality contributes to approximately 15% and 8% of overall failure-to-rescue (FTR)-related incidence and mortality (13.8 and 140 per 1000 patients, respectively).[45 46] Despite the fact that our study and the U.S. study used the identical measure defined by AHRQ,[23] the discrepancies and coding practices between the U.S. (ICD-9-CM) and Australia (ICD-10-AM) may, in part, have contributed to the difference. It was shown that accuracy of VTE coding can be improved by the adoption of extended codes developed in the revised ICD-9-CM. [47]

In a recent Organization for Economic and Co-Operation and Development (OECD) report, Australian-wide incidence were 0.97 and 1.26 per 1000 patients in 2009 and 2012 respectively, placing Australia among three nations (Australia, Slovenia and the U.S.) with the highest incidence of approximately one per a thousand surgical patients or more within the last decade.[48] Our observed rate for NSW hospitals was nearly double that of the OCED provided Australian rates, possibly due to the fact that we studied only elective surgical patients from acute public hospitals. Such cross-nations reports provide a platform for health service comparisons and the study of longitudinal variations. However, internal and external comparability of OCED results may be affected by the heterogeneity and biases of the different nation's coding systems.

Despite continued poor compliance with VTE prevention guidelines and VTE preventative measures,[49-52] post-operative VTE incidence in U.S. hospitals almost halved between 2007-2011.[24 44] In Australia, given the overt gap between evidence and practice of VTE prevention protocols,[53 54] the National Institute of Clinical Studies (NICS) launched a VTE prevention program in 85 public and private hospitals across Australia between 2005-2008 which resulted in

increased awareness of and adherence with VTE prevention guidelines.[2 55] However, we found an increasing trend in NSW post-operative VTE incidence rate within 2002-2009, with an approximate 4% annual increase and total increase of 30%, mostly contributed by the higher incidence in the smaller hospital peer groups (237%) compared to the large teaching hospital group (19%). The reason for this increase is unclear.

Our finding of a higher incidence of VTE and VTE associated mortality with increasing age is similar that observed by others.[29 56-58] Ageing previously accepted as a major contributing factor to the increasing trends in VTE rates for admitted patients in Australian hospitals.[3] However, we have taken into account patient characteristics including age as well as surgery type and demonstrated an adjusted increasing trend for surgical patients, despite the observed decreasing trends in proportions of AAA repair and orthopaedic surgical procedures (Appendix 2) known with high post-operative VTE risks (Table 1).[1] Notably, the steadily increasing VTE incidences among patients who underwent other surgical procedures mainly contributed to the observed overall trend (Figure 3). More research is required to examine the contributing factors for such a difference among different surgical procedures. In particular, comorbidity-specific analysis at hospital level is encouraged to minimise potential biases reported elsewhere.[39-41]

Although other studies suggest gender may not be a significant risk factor for VTE,[28 29 59] we found males were less likely to develop VTE complications, but more likely to subsequently die. We did not separately explore DVT and PE incidence and associated deaths between genders; but our higher mortality risk for males can be explained by the estimated higher odds of PE (vs. DVT which has a lower risk of death[29 59] for males compared to females (1.87 vs. 1.02 respectively) in Australian hospitals during our study period.[3]

Variation in the application of VTE prevention guidelines and other quality initiatives may have contributed to the differences in outcomes amongst the hospitals in our study. Smaller, district 1 and 2 peer groups hospitals, had a significantly lower VTE incidence rate compared to larger hospitals in NSW. This was in contrast with other studies which showed that larger hospitals have a lower mortality following major procedures, such as orthopaedic surgeries[60 61] and post-operative complications such as VTE.[62] A possible explanation for this discrepancy is that principal referral hospitals undertook higher risk patients and surgical complexity than the smaller district hospitals. Geographical variations in coding,[39-41] underreporting of VTE due to mis-coding to a more general cardiovascular item,[3 63] and high diagnosis likelihood of high-risk but asymptomatic post-operative patients[64] may also have contributed to elevated VTE rates in major hospitals. We did not observe differences between NSW hospital peer groups for VTE mortality, nor did other studies for

FTR rates. However, we did observe greater variation in VTE mortality within peer groups comprising smaller sized hospitals in comparison to larger principal referral hospitals.

Our study showed a significant performance difference between hospitals, within each hospital peer group, with the highest and those with the lowest VTE incidence and associated mortality. Similarly, the association between the two outcomes also varied across groups. Smaller hospitals (district groups 1 and 2) exhibited larger differences in both outcomes, suggesting a greater variability of patient care practice and outcomes amongst this group of hospitals and the greater potential for intervention aimed at VTE prevention and treatment for this group. We also noted a positive association between VTE incidence and VTE mortality amongst smaller size hospital groups. In contrast, larger NSW hospitals tended to have a higher VTE incidence but lower VTE associated mortality, suggests that there may be a volume-outcome relationship or a greater adherence to evidence-based prevention and treatment guidelines that may explain this better VTE associated mortality. Interestingly, if the higher incidence of VTE alone was used as a measure of failure-to-prevent, these hospitals may be considered to have performed poorly overall, despite the better VTE associated mortality. Conversely, if the higher incidence rates of VTE were largely due to patient selection and case-mix, these hospitals could be considered as better quality hospitals having a lower failure-to-rescue rate with better treatment outcomes. Further investigation into the factors that may explain these differences and the ideal reporting measures is warranted.

Our study raised several important policy implications. Firstly, despite the fact that national and state agencies had developed evidence-based guidelines, such as the Clinical Excellence Commission of NSW "Medication Safety",[65] in which VTE prevention practices were promoted and related incidents evaluated, the increasing incidence of VTE and unchanged VTE mortality question the effectiveness of current national policy and local programs in reducing VTE incidence and mortality. Secondly, the development of systematic local program based on relevant international experience in successfully reducing VTE rate and its related mortality needs urgent policy action. Thirdly, the large variability of VTE rate and its related mortality between and within different hospital peer groups suggests that there is room for improvement in both the prevention and treatment of VTE and that VTE still remains a preventable complication. Lastly, as an important indicator of the quality of care, the level of standardised reporting of VTE in Australia should be explored.

The strengths of our study are that it is the first population-based observational study across all acute public hospitals within the one (i.e. NSW) health region. We used a standardised measure and presented both incidence rates of VTE and VTE associated mortality, thus enabling to differentiate between the two outcome measures and allow for international comparisons. Limitations of our study

include that we specifically studied only elective surgical patients according to AHRQ definitions; whereas the analyses of all patient populations may provide addition insight. Future research needs to provide more evidence on the whole inpatient population. We also may have under-reported our findings because of possible coding discrepancies. Nevertheless, this study reinforced the importance of developing measures for combating post-operative VTE, and the continual monitoring and public reporting VTE incidence and mortality.[2 66]

CONCLUSION

The significant increase in VTE incidence among surgical patients over an eight-year period, and persisting level of VTE associated mortality, highlights the need for urgent policy interventions. The significant variation for both outcomes between, and within, different hospital peer groups suggests room for improvement in both the prevention and treatment of VTE. Routine measurement and disclosure of both VTE incidence and associated mortality can provide policy-makers, clinicians and researchers with opportunities to monitor and adjust for performance.

CONTRIBUTORS

Conceived and designed the study: HA, JC, AF, and KH. Prepared the data and performed the analyses: HA, JC, and LO. Wrote the paper: HA, JC, SH, AF, and KH.

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COMPETING INTERESTS

Authors had no conflict of interest.

PROVENANCE AND PEER REVIEW

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No additional data are available.

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FIGURE LEGENDS

Figure 1. Adjusted trends of post-operative VTE and post-VTE death incidence rates (per 1000 elective surgical patients, and 1000 patients with post-operative VTE respectively) over the study period. Rates were estimated by multiplying incidence rate ratio (obtained from the Poisson mix model) and crude risk at the reference year (2002).

Figure 2. Hospital peer group-specific adjusted trends of post-operative VTE (left panel) and post-VTE death (right panel) incidence rates (per 1000 elective surgical patients, and 1000 patients with post-operative VTE respectively) over the study period. Rates were estimated by multiplying incidence rate ratio (obtained from the Poisson mix model including an interaction term for "hospital peer group × year") and crude risk of the reference hospital group (Principal referral) at the reference year (2002).

Figure 3. Surgical procedure-specific adjusted trends of post-operative VTE incidence rates (per 1000 elective surgical patients) over the study period. Rates were estimated by multiplying incidence rate ratio (obtained from the Poisson mix model including an interaction term for "surgery type × year") and crude risk of the reference surgery group (AAA repair) at the reference year (2002).

Title: Rate of venous thromboembolism among surgical patients in Australian hospitals: A large retrospective cohort study~~population based study~~

Running title: Post-operative venous thromboembolism in Australia

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Rate of Venous Thromboembolism among Surgical Patients in Australian Hospitals: A ~~Population-based~~Large Retrospective Cohort Study

ABSTRACT

Objectives: Despite the burden of venous thromboembolism (VTE) among surgical patients on health systems in Australia, data on VTE incidence and its variation within Australia is lacking. We aim to explore VTE incidence and associated mortality rates, and their trends and variations across Australian acute public hospitals.

Setting: A large retrospective cohort ~~population based~~ study using all elective surgical patients in 82 acute public hospitals during 2002-2009 in New South Wales, Australia.

Participants: Patients who had elective surgery within two days of admission, aged between 18 – 90 years, and were not transferred to another acute care facility; 4,362,624 patients were included.

Outcome Measures: VTE incidents were identified by secondary diagnostic codes. Poisson mixed models were used to derive adjusted incidence rates and rate ratios (IRR) in presence of patient and hospital characteristics.

Results: Two per 1000 patients developed post-operative VTE. VTE increased by ~~28~~30% (IRR=1.~~28~~30, CI: 1.~~17~~19-1.4~~0~~2) over the study period. Differences in the VTE rates, trends between hospital peer groups and between hospitals with the highest and those with the lowest rates were significant (between-hospital variation). Smaller hospitals, accommodated in two peer groups, had the lowest overall VTE rates (IRR=0.56:0.~~32~~33-~~1~~0.~~00~~95; IRR=0.3~~2~~7:0.~~18~~23-0.~~55~~61) and exhibited a greater increase (~~61~~64% and ~~241~~237% vs. ~~17~~19%) over time and greater between-hospital variations compared to larger hospitals (IRR=~~98~~.~~90~~64:~~76~~.~~16~~23-~~13~~11.~~67~~98; IRR=8.~~86~~92:5.~~45~~49-14.~~40~~ 49 vs. IRR=~~43~~.~~46~~70:~~43~~.~~40~~32-4.~~97~~12). Mortality among patients with post-operative VTE was 8% and remained stable over time (IRR=~~1~~0.~~01~~98:0.~~97~~95-1.~~04~~02). No differences in post-VTE death rates and trends were seen between hospital groups; however larger hospitals exhibited less between-hospital variations (IRR=~~1~~1.~~99~~78:1.~~43~~30-2.~~77~~44) compared to small hospitals (IRR~~=~~>~~37~~23)~~.00:10.11-101.35)~~. Hospitals performed differently in prevention versus treatment of post-operative VTE.

Conclusions: The incidence of VTE is increasing and there is large variation between- and within-hospital peer groups suggesting a varied compliance with VTE preventative strategies and the potential for targeted interventions and quality improvement opportunities.

ARTICLE SUMMARY

Article focus

- To evaluate rates and trends of post-operative VTE incidence and subsequent mortality within Australian hospitals
- To demonstrate and compare variations of VTE incidence and subsequent deaths between hospitals

Key messages

- Post-operative VTE incidence rate was two per 1000 patients. It increased by 28% over the study period. Post-VTE mortality rate was 8% and remained stable over time.
- Smaller hospitals had lower VTE rates but exhibited a greater increase over time and greater between-hospital variations compared to larger hospitals. They also exhibited greater between-hospital variations in post-VTE death rates.

Strengths and limitations of this study

- This study benefited from a large cohort ~~population based~~ design within the largest health jurisdiction in Australia.
- Employment of standardised and broadly-applied VTE measures facilitated local and international comparisons and benchmarking.
- Demonstration of trends and variations in VTE measures reflected effectiveness of systematic interventions and revealed opportunities for further improvement and actions at local and regional levels.
- This study was limited to VTE incidence among elective surgical patients. Analysis of all patient populations may provide addition insight.
- The obtained rates may have under-estimated due to possible coding discrepancies.

INTRODUCTION

Venous thromboembolism (VTE), comprised of deep-vein thrombosis (DVT) and pulmonary embolism (PE), can cause long-term comorbidities or death[1 2] and incur significant financial burden on healthcare systems.[3 4] It accounts for nearly 10% of all deaths in U.S. [5 6] and Australian hospitals,[7 8] and is amongst the top five most common causes of hospital-related deaths in both countries.[3 9] However, VTE is also the most common preventable cause of hospital deaths.[10-13] A significant decrease in VTE incidents has been reported where efficacious and cost-effective treatments (ie. pharmacological and mechanical prophylaxis) were used for both medical and surgical patients.[1 12 14-19] Accordingly, several evidence-based VTE prevention and treatment guidelines were developed[1 9 20] and related measures were adopted among quality of care indices for accreditation, quality improvement and benchmarking purposes.[21-23]

The Agency for Healthcare Research and Quality (AHRQ) listed post-operative VTE complications and subsequent death as a component of failure-to-rescue (FTR) among patient saftey indicators (PSI#12 and PSI#4-2 respectively), which are routinely being monitored and publically reported.[23 24] Reports showed that the post-operative VTE incidence rates have nearly halved in U.S. hospitals in recent years,[24 25] and post-VTE mortality rate declined by a third within a decade since the mid-90s.[26] These rate decreases may be, in part, due to the implementation of post-operative VTE prevention protocols,[27] however substantial variation in post-operative VTE incidence rate was also evident among U.S. hospitals.[25] Although patients case mix and surgery types may play a role in such differences,[6 28 29] the variation of VTE incidence among the same type of hospitals over time and within the group may reflect the success of quality improvement interventions and demonstrate the potential for further development.[30 31]

Few Australian studies have reported VTE incidence,[3 8 32] and the measures of VTE used in these studies varied making comparison difficult. Consequently, we employed the internationally-recognised AHRQ measures for post-operative VTE, and subsequent mortality, to explore the trend of the incidence rates and their variations among admitted surgical patients in acute public hospitals across New South Wales (NSW), Australia (2002-2009).

METHODS

Data source and study population

New South Wales is the largest health jurisdiction in Australia with approximately 497 healthcare facilities and a population of over seven million people. We used records from the NSW Admitted

Patient Data Collection (APDC) database, which includes all admitted patient services provided by NSW public and private healthcare facilities. The APDC includes information on patient demographics, medical conditions and procedures, hospital characteristics, and separations (discharges, transfers and deaths) from all public and private hospitals (as well as day procedure centres) in NSW. The medical records for each episode of care in the APDC were assigned with codes based on the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification (ICD-10-AM) 4th edition.[33] Of admissions at 497 healthcare facilities across NSW between 1st January 2002 to 31st December 2009, we included all 82 NSW acute public hospitals (9,221,128 admissions; 57.4%) in our study. Two children's hospitals and one other hospital (data was unavailable) were excluded We restricted our study to only elective surgical patients and applied the same AHRQ inclusion criteria[23] for patients who had elective surgery within two days of admission, aged between 18 – 90 years (inclusive), and were not transferred to another acute care facility (4,362,624 episodes (47.3%)). Ethical approval was obtained from the University of NSW Human Research Ethics Committee (LNR/11/CIPHS/64).

Measures and covariates

Patients who developed VTE were identified by secondary diagnostic codes (ICD-10-AM) translated from the AHRQ definition (ICD-9-CM) by Victorian Government Health Information.[34] We employed the term "post-operative VTE" from the Australian version of patient safety indicators (AusPSI)[35] instead of "peri-operative VTE" developed by AHRQ. In combination with discharge status, patients post-VTE outcomes were categorised as survival or death. VTE and related death rates were presented as incidences per 1000 admissions within each year between 2002 and 2009, inclusively.

Two sets of patient- and hospital-related covariates were considered. Patient demographic variables included age, gender, country of birth, marital status, patient socio-economic status, and principle diagnostic disease groups (the ten most common) within the study population. We utilised a postcode-level advantage and disadvantage index of Socio-Economic Indices for Areas (SEIFA) with the lower values indicating more disadvantaged areas.[36] SEIFA scores were categorised into four classes (1st quartile = most disadvantaged areas and 4th quartile = most advantaged areas). The disease groups were identified using principle diagnostic codes (ICD-10-AM) at admissions through the methodology develop by Quan et al..[37] Using relevant procedure codes from ICD-10-AM (Appendix 1), we defined six major surgical procedures including coronary-artery bypass graft (CABG), abdominal aortic aneurysm (AAA) repair, total hip replacement, total knee replacement, cholecystectomy, and other surgical procedures.

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Hospital covariates included the local health district (metropolitan, rural and regional NSW) and peer group (A1: principal referral group, usually teaching hospitals; A3: ungrouped acute; B: major metropolitan and non-metropolitan; C1: district group 1; and, C2: district group 2). Hospital peer groups contained similar type and sized hospitals, ranging from those treating more than 25,000 acute case-mix weighted separations per annum in principal referral groups through to treating 2,000^{+} (but less than 5,000) acute case-mix weighted separations per annum in district group 2.[38]

Statistical analysis

We employed Poisson mixed models to evaluate adjusted incidence rates and rate ratios for study outcomes after including all patients and hospital-related characteristics. A random intercept term was utilised to incorporate any clustering effect at hospital-level. To investigate the temporal behaviour of the outcomes, calendar years were entered into the model as indicator variables, with 2002 as the reference year. A model with the year as a continuous variable was also examined for linear trends. We derived hospital peer group and surgery type trends using ~~an~~ interaction effects (year and hospital peer group; year and surgery type) in ~~a~~ separate models. Adjusted incidence rates for specific years were derived by multiplying yearly-adjusted risk ratios to the crude risks observed in the reference year.

We initially examined the Elixhauser and the Charlson Index comorbidities based on the ICD-10 coding scheme,[37] however we did not include either of them in the models given an unexpected drop in the comorbidity index among our study population in recent years (Appendix 2) and also recent reports that these indices may introduce misleading results possibly due to geographical variations and biases in the coding.[39-41] To study the variation of outcomes across hospitals within each hospital group, hospital-specific random intercept components were extracted from Poisson mixed models constructed for each hospital group, then ranked and categorised into five classes at 20% incremental quintiles. To obtain adjusted differences between those with the highest and those with the lowest VTE incidence, the adjusted classes were entered into a Poisson model including patient characteristics covariates. We used Pearson correlation to assess the association of hospital performances between VTE and post-VTE deaths, based on the hospital-specific random intercepts. All analyses were performed in R package version 3.0.0[42] and Stata^{TM} 11.0.[43]

RESULT

Error! Reference source not found. summarised the study population by outcomes across hospital and patient characteristics and related statistics. Of the 4,223,317 (45.8% of all admissions with no missing information) elective surgical admissions during 2002-2009, 8,451 patients developed either

DVT or PE after surgery, resulting in an incidence rate of 2 per 1000 surgical patients. Among them, ~~671~~ 673 died prior to discharge (8%); 79.6 per 1000 patients with post-operative VTE. Compared to females, males tended to have a lower risk of post-operative VTE (IRR=0.~~87~~91); however, they were more likely to die (IRR=1.~~23~~19) following a VTE. Older patients were exposed to higher risks of VTE and death after surgery. Married patients and those who were born in Europe (except the UK), Asia and North Africa experienced a lower risk of post-operative VTE compared to their counterparts but a similar risk of post-VTE death.

Patients admitted with malignancy and congestive heart failure had the highest VTE and hospital mortality rates. Patients who underwent total knee replacement, AAA repair and total hip replacement surgeries had higher risk of VTE, respectively; however, post-VTE mortality was lower among orthopaedic surgical patients compared to other procedures. Higher socio-economic status (quartiles of SEIFA) of patients was associated with a lower risk of VTE. There was no difference in mortality for patients residing in advantaged and disadvantaged areas. Patients from principal referral hospitals were more likely to acquire VTE in comparison to the patients from district hospitals (IRR= 0.56 and 0.~~32~~ 37 for group 1 and 2 hospitals respectively). No differences in outcomes were observed between metropolitan and non-metropolitan hospitals.

Post-operative VTE incidence rate significantly increased over the study period by ~~28~~30%, from 1.77 per 1000 patients in 2002 to 2.~~20~~ 30 in 2009 (Figure 1). Despite some fluctuation, all hospital peer groups exhibited similar increasing trends in post-operative VTE incidence over the study period after adjustment for patient demographics (Figure 2), ranging from ~~17~~19% (2.~~55~~ 58 vs. 2.17) in principal referral hospitals to ~~241~~237% (1.~~23~~ 21 vs. 0.36) in district group 2. Surgery-specific VTE rates for the five procedures exhibited high fluctuations and insignificant trends, whereas the other surgery group showed a steady increasing trend of 38% (3.01 vs. 2.18) over the study period (Figure 3). Post-VTE mortality fluctuated between 68 to 97 cases per 1000 patients over the study period with no significant change after adjusting for confounders overall (Figure 1) and at hospital peer group level (Figure 2). Mortality tended to be stable across hospital peer groups as between-group variation of mortality reduced over the study period. No surgery-specific trend analysis was conducted due to small number of post-DVT deaths per annum.

The incidence rate ratios between those hospitals with the lowest, and those with the highest rate, was larger in VTE related mortality than in VTE and varied across hospital peer group (**Error! Reference source not found.**). For VTE, the difference in rate is ~~less than~~ less than ~~five~~four-fold in the principal referral and ~~ungrouped acute hospital~~ major peer groups (include large hospitals) but at least eight-fold in ~~other~~ district peer groups (include small hospitals). Similarly, the difference in rate is larger in

district group 1 and 2 (IRR=~~37~~23 and 38) compared to principal referral (IRR=~~2~~1.7) and major metropolitan/non-metropolitan hospitals (IRR=15) for VTE related deaths. The close to significant ~~significant~~ negative correlation (-0.~~62~~45, P-value=0.057) for principal referral hospitals implied that hospitals with the highest post-operative VTE rate tended to have a lower rate of subsequent death. In contrast, within district group 2 (0.~~40~~41), hospitals with higher VTE rates tended to also have the highest post-VTE death rates. There were no such associations within other peer groups.

Table 1. Study population, Incidence rates (IR) and adjusted incidence rate ratios (IRR) of surgical patients who developed VTE and died, stratified by patient and hospital characteristics.

Characteristics	Surgical patients n (%)	VTE			VTE associated death			
		Frequency (%)	IR	IRR (95% CI)	Frequency (%)	IR	IRR (95% CI)	
Sex								
Female	2280384 (54.00)	4626 (54.74)	2.03	1.00	330 (49.03)	71.34	1.00	
Male	1942933 (46.00)	3825 (45.26)	1.97	0.90 0.87 (0.86-0.94)(0.83-0.91)	343 (50.97)	89.67	1.191. 23 (1.02-1.40)(1.05-1.44)	***
Age								
>=18yr & <35yr	738382 (17.48)	487 (5.76)	0.66	0.21 0.18 (0.19-0.23)(0.17-0.20)	11 (1.63)	22.59	0.200. 21 (0.11-0.37)(0.11-0.39)	***
>=35yr & <55yr	1013921 (24.01)	1308 (15.48)	1.29	0.42 0.38 (0.40-0.45)(0.36-0.41)	82 (12.18)	62.69	0.580. 59 (0.45-0.74)(0.46-0.76)	***
>=55yr & <75yr	1595024 (37.77)	3538 (41.86)	2.22	0.66 0.67 (0.63-0.70)(0.64-0.71)	290 (43.09)	81.97	0.850. 81 (0.72-1.01)(0.68-0.96)	*
>=75yr & <90	875990 (20.74)	3118 (36.90)	3.56	1.00	290 (43.09)	93.01	1.00	
Marital status								
Married	2548508 (60.34)	4667 (55.22)	1.83	1.00	381 (56.61)	81.64	1.00	
Single	1674809 (39.66)	3784 (44.78)	2.26	1.16 1.16 (1.11-1.21)(1.11-1.21)	292 (43.39)	77.17	1.010. 99 (0.86-1.18)(0.84-1.16)	
Country of birth								
Australia and New Zealand	2839135 (67.23)	5858 (69.32)	2.06	1.00	479 (71.17)	81.77	1.00	
UK, US & Canada	239088 (5.66)	645 (7.63)	2.70	1.06 1.09 (0.97-1.15)(1.00-1.18)	53 (7.88)	82.17	0.950. 95 (0.72-1.27)(0.71-1.27)	
Non-English Europe	447239 (10.59)	1046 (12.38)	2.34	0.74 0.73 (0.69-0.80)(0.68-0.79)	80 (11.89)	76.48	0.910. 88 (0.71-1.16)(0.68-1.12)	
North Africa	130938 (3.10)	139 (1.64)	1.06	0.47 0.45 (0.40-0.56)(0.38-0.53)	9 (1.34)	64.75	0.870. 88 (0.45-1.70)(0.45-1.71)	
Asia	179725 (4.26)	193 (2.28)	1.07	0.45 (0.39-	16 (2.38)	82.90	1.090. (0.66-	

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Others	387192 (9.17)	570 (6.74)	1.47	0.58 0.57	(0.53-0.64)(0.52-0.62)	****	36 (5.35)	63.16	0.950.88	(0.67-1.35)(0.62-1.24)
Major surgical procedure										
AAA repair	1744 (0.04)	26 (0.31)	14.91	1.00			6 (0.89)	230.77	1.00	
CABG	10529 (0.25)	52 (0.62)	4.94	0.37	(0.23-0.60)	**	7 (1.04)	134.62	0.69	(0.23-2.10)
Cholecystectomy	50145 (1.19)	42 (0.50)	0.84	0.09	(0.05-0.15)	**	6 (0.89)	142.86	0.70	(0.22-2.22)
Total hip replacement	18771 (0.44)	207 (2.45)	11.03	0.74	(0.49-1.11)		4 (0.59)	19.32	0.12	(0.03-0.44) **
Total knee replacement	29428 (0.70)	798 (9.44)	27.12	1.76	(1.19-2.61)	**	3 (0.45)	3.76	0.03	(0.01-0.11) **
Other	41 12700 (97.38)	7326 (86.69)	1.78	0.17	(0.11-0.24)	**	647 (96.14)	88.32	0.52	(0.23-1.19)
Major principle diagnostic diseases†										
Cardiac arrhythmias	25953 (0.61)	75 (0.89)	2.89	-			2 (0.30)	26.67	-	
Chronic pulmonary disease	11558 (0.27)	69 (0.82)	5.97	-			6 (0.89)	86.96	-	
Coagulopathy	3908 (0.09)	37 (0.44)	9.47	-			2 (0.30)	54.05	-	
Congestive heart failure	6765 (0.16)	85 (1.01)	12.56	-			17 (2.53)	200.00	-	
Diabetes with chronic complication	33541 (0.79)	79 (0.93)	2.36	-			11 (1.63)	139.24	-	
Malignancy including lymphoma & leukaemia	150962 (3.57)	1070 (12.66)	7.09	-			182 (27.04)	170.09	-	
Metastatic solid tumour	19699 (0.47)	291 (3.44)	14.77	-			67 (9.96)	230.24	-	
Peripheral vascular disease	15993 (0.38)	141 (1.67)	8.82	-			10 (1.49)	70.92	-	
Renal failure	1385753 (32.81)	42 (0.50)	0.03	-			1 (0.15)	23.81	-	
Rheumatoid arthritis/collagen vascular disease	10748 (0.25)	40 (0.47)	3.72	-			1 (0.15)	25.00	-	
Year										
2002	431184 (10.21)	763 (9.03)	1.77	1.00			65 (9.66)	85.19	1.00	
2003	438058 (10.37)	780 (9.23)	1.78	1.01 1.01	(0.92-1.12)(0.92-1.12)		53 (7.88)	67.95	0.850.84	(0.59-1.22)(0.58-1.21)
2004	462451 (10.95)	878 (10.39)	1.90	1.09 1.09	(0.99-1.20)(0.99-1.20)		65 (9.66)	74.03	0.820.83	(0.58-1.16)(0.59-1.18)
2005	508097 (12.03)	1038 (12.28)	2.04	1.17 1.18	(1.07-1.29)(1.08-1.30)	****	75 (11.14)	72.25	0.770.78	(0.55-1.08)(0.56-1.09)

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2006	550688 (13.04)	1062 (12.57)	1.93	1.11 1.12	(1.01-1.22)(1.02-1.23)	**	103 (15.30)	96.99	1.021. 01	(0.74-1.40)(0.74-1.39)
2007	591973 (14.02)	1223 (14.47)	2.07	1.22 1.22	(1.12-1.34)(1.11-1.33)	****	87 (12.93)	71.14	0.720. 75	(0.52-1.01)(0.54-1.04)
2008	607631 (14.39)	1313 (15.54)	2.16	1.27 1.26	(1.16-1.38)(1.15-1.38)	****	112 (16.64)	85.30	0.900. 94	(0.66-1.23)(0.69-1.28)
2009	633235 (14.99)	1394 (16.50)	2.20	1.30 1.28	(1.19-1.42)(1.17-1.40)	****	113 (16.79)	81.06	0.830. 87	(0.60-1.13)(0.63-1.18)
Year-linear trend	-	-	-	1.03 04	(1.0203-1.0405)	**	-	-	0.981. 01	(0.95-1.02)(0.97-1.04)
Quartiles of SEIFA										
1st quartile (most disadvantaged)	1089833 (25.81)	2308 (27.31)	2.12	1.00			187 (27.79)	81.02	1.00	
2nd quartile	1084727 (25.68)	1981 (23.44)	1.83	0.88 0.88	(0.82-0.94)(0.82-0.93)	****	169 (25.11)	85.31	0.960. 95	(0.78-1.20)(0.76-1.18)
3rd quartile	1074283 (25.44)	2088 (24.71)	1.94	0.76 0.75	(0.72-0.81)(0.71-0.80)	****	175 (26.00)	83.81	1.041. 01	(0.84-1.30)(0.81-1.26)
4th quartile (most advantaged)	974474 (23.07)	2074 (24.54)	2.13	0.70 0.66	(0.65-0.75)(0.62-0.71)	****	142 (21.10)	68.47	0.980. 98	(0.77-1.26)(0.77-1.26)
Peer hospital groups										
Principal referral	2269392 (53.73)	5141 (60.83)	2.27	1.00			381 (56.61)	74.11	1.00	
Ungrouped acute	133465 (3.16)	380 (4.50)	2.85	1.20 1.05	(0.54-2.66)(0.44-2.50)		43 (6.39)	113.16	0.940. 93	(0.37-2.39)(0.32-2.70)
Major metro- & non-metropolitan	1140036 (26.99)	2125 (25.14)	1.86	0.84 0.85	(0.54-1.31)(0.52-1.39)		183 (27.19)	86.12	0.960. 88	(0.60-1.55)(0.51-1.52)
District group 1	346910 (8.21)	484 (5.73)	1.40	0.56 0.56	(0.33-0.95)(0.32-1.00)	**	42 (6.24)	86.78	0.990. 94	(0.54-1.83)(0.47-1.89)
District group 2	333514 (7.90)	321 (3.80)	0.96	0.37 0.32	(0.23-0.61)(0.18-	****	24 (3.57)	74.77	0.740. 77	(0.38-1.44)(0.37-

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				~~0.55)~~				~~1.61)~~
Local health district								
Metropolitan	2720690 (64.42)	5882 (69.60)	2.16	1.00	430 (63.89)	73.10	1.00	
Rural & Regional NSW	1502627 (35.58)	2569 (30.40)	1.71	0.74 ~~0.70~~ (0.52-1.05) ~~(0.48-1.02)~~	243 (36.11)	94.59	1.26 ~~1.32~~ (0.82-1.92) ~~(0.82-2.13)~~	
Total	4223317	8451	2.00	-	673	79.64	-	

139,307 (3.2%) cases were excluded due to missing or unknown items.

Incidence rates (IR) are crude and reported per 1000 patients.

Risk ratios (RR) and related confident intervals (CI) were obtained using a Poisson mixed model.

CABG: Coronary Artery Bypass Graft; AAA repair: Abdominal Aortic Aneurysm repair.

~~Incidence rates (IR) are crude and reported per 1000 patients.~~

~~Risk ratios (RR) and related confident intervals (CI) were obtained using a Poisson mixed model.~~

† No RR is reported since this characteristic has not been included in the Poisson mixed model.

* Significant at 5%; ** significant at 1%.

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Table 2. Incidence rates (IR), adjusted incidence rate ratios (IRR) and association of outcomes between the best and worst performers (top and bottom 20% quintiles) within hospital peer groups

Hospital peer group	Hospital n	VTE				Post-VTE death				Correlation coefficient (95% CI)	
		Lowest (IR)	Highest (IR)	IRR (95% CI)		Lowest (IR)	Highest (IR)	IRR (95% CI)			
Principal referral	1417	1.2424	4.9700	43.46 (43.0032-704.9712)	**	3843.60 58	124131. 1712	1.997 (1.4330-82.7744)	**	-0.6245 (-0.8679, -0.1301)	*
~~Ungrouped acute† §~~	~~3~~	~~0.65~~	~~7.30~~	~~9.91 (6.53-15.02)~~	~~**~~	~~0.00~~	~~142.36~~	~~-~~		~~-~~	
Major metro- & non-metropolitan	22	0.891.00	2.8799	43.56 (3.9233-8554.3146)	**	16.80	148162. 8130	15.084 (6.2745-836637.2312)	**	0.1415 (-0.3028,0.5354)	
District group 1	13	0.42	3.71	98.90 (76.1623-6413311.6798)	**	13.88	242.71	3738.0 (10.1125-002101140.3594)	**	-0.3637 (-0.76,0.2422)	
District group 2†	30	0.22	2.15	8.869 (5.4549-214.4049)	**	016.006 6	109104. 1997	-23.26 (2.94-183.50)	**	0.404 (0.0305,0.6718 68)	*

Incidence rates (IR) are crude and reported per 1000 patients.
Risk ratios (RR) and related confident intervals (CI) were obtained using a Poisson model and adjusted for patient characteristics. Those hospitals with the lowest rate were set as the reference level.
† Ungrouped acute group was removed from analysis due to small number of hospitals within this group.
~~No RR is reported for Post-VTE death due to zero incidences in the reference level.~~
~~§ No correlation coefficient is reported due to small number of hospitals within this group.~~
* Significant at 5%; ** significant at 1%.

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DISCUSSION

In this large cohort study~~population based study~~, of elective surgical patients, from all NSW acute public hospitals, over an 8 year period, we found that the incidence of VTE to be two of 1000 elective surgical admissions, and VTE associated mortality to be 8%. The adjusted incidence of VTE increased significantly over the study period (~~28~~30%), with no change in mortality. There were significant differences in incidence of VTE between hospital peer groups and between hospitals with the lowest and those with the highest rate. Principal referral hospitals exhibited a higher overall incidence, but lower intragroup variation compared to other peer groups. Principal referral hospitals with a higher incidence of VTE also tended to have a lower VTE-related mortality.

The incidence of post-operative VTE in NSW hospitals was less than half that of. U.S. hospitals within a similar period (4.5 or more per 1000 patients in 2010 and prior),[25 44] but with a similar VTE associated mortality (83 vs. 79 per 1000 patients). [25] Based upon our findings, VTE incidence and associated mortality contributes to approximately 15% and 8% of overall failure-to-rescue (FTR)-related incidence and mortality (13.8 and 140 per 1000 patients, respectively).[45 46] Despite the fact that our study and the U.S. study used the identical measure defined by AHRQ,[23] the discrepancies and coding practices between the U.S. (ICD-9-CM) and Australia (ICD-10-AM) may, in part, have contributed to the difference. It was shown that accuracy of VTE coding can be improved by the adoption of extended codes developed in the revised ICD-9-CM. [47]

In a recent Organization for Economic and Co-Operation and Development (OECD) report, Australian-wide incidence were 0.97 and 1.26 per 1000 patients in 2009 and 2012 respectively, placing Australia among three nations (Australia, Slovenia and the U.S.) with the highest incidence of approximately one per a thousand surgical patients or more within the last decade.[48] Our observed rate for NSW hospitals was nearly double that of the OCED provided Australian rates, possibly due to the fact that we studied only elective surgical patients from acute public hospitals. Such cross-nations reports provide a platform for health service comparisons and the study of longitudinal variations. However, internal and external comparability of OCED results may be affected by the heterogeneity and biases of the different nation's coding systems.

Despite continued poor compliance with VTE prevention guidelines and VTE preventative measures,[49-52] post-operative VTE incidence in U.S. hospitals almost halved between 2007-2011.[24 44] In Australia, given the overt gap between evidence and practice of VTE prevention protocols,[53 54] the National Institute of Clinical Studies (NICS) launched a VTE prevention program in 85 public and private hospitals across Australia between 2005-2008 which resulted in

increased awareness of and adherence with VTE prevention guidelines.[2 55] However, we found an increasing trend in NSW post-operative VTE incidence rate within 2002-2009, with an approximate ~~3~~4% annual increase and total increase of ~~28~~30%, mostly contributed by the higher incidence in the smaller hospital peer groups (~~241~~237%) compared to the large teaching hospital group (~~17~~19%). The reason for this increase is unclear.

Our finding of a higher incidence of VTE and VTE associated mortality with increasing age is similar that observed by others.[29 56-58] Ageing previously accepted as a major contributing factor to the increasing trends in VTE rates for admitted patients in Australian hospitals.[3] However, ~~despite that~~ we have taken into account patient ~~demographic~~ characteristics including age as well as surgery type and demonstrated an adjusted increasing trend for surgical patients, despite the observed decreasing trends in proportions of AAA repair and orthopaedic surgical procedures (Appendix 2) known with high post-operative VTE risks (Table 1).[1]~~other factors such as patient mix and surgery type may also contribute to our observed trend. For example, the increase in major surgeries such as hip (39%) and knee (72%) replacement procedures with the highest post-operative VTE risk between 2002 and 2010 in Australia~~[1 59 60]~~ are likely to have contributed to the upward trend in VTE rates.~~ Notably, the steadily increasing VTE incidences among patients who underwent other surgical procedures mainly contributed to the observed overall trend (Figure 3). More research is required to examine the contributing factors for such a difference among different surgical procedures~~effect of these factors~~. In particular, comorbidity--specific analysis at hospital level is encouraged to minimise potential biases reported elsewhere.[39-41]

Although other studies suggest gender may not be a significant risk factor for VTE,[28 29 59] we found males were less likely to develop VTE complications, but more likely to subsequently die. We did not separately explore DVT and PE incidence and associated deaths between genders; but our higher mortality risk for males can be explained by the estimated higher odds of PE (vs. DVT which has a lower risk of death[29 59] for males compared to females (1.87 vs. 1.02 respectively) in Australian hospitals during our study period.[3]

Variation in the application of VTE prevention guidelines and other quality initiatives may have contributed to the differences in outcomes amongst the hospitals in our study. Smaller, district 1 and 2 peer groups hospitals, had a significantly lower VTE incidence rate compared to larger hospitals in NSW. This was in contrast with other studies which showed that larger hospitals have a lower mortality following major procedures, such as orthopaedic surgeries[60 61] and post-operative complications such as VTE.[62] A possible explanation for this discrepancy is that principal referral hospitals undertook higher risk patients and surgical complexity than the smaller district hospitals.

Geographical variations in coding,[39-41] underreporting of VTE due to mis-coding to a more general cardiovascular item,[3 63] and high diagnosis likelihood of high-risk but asymptomatic post-operative patients[64] may also have contributed to elevated VTE rates in major hospitals. We did not observe differences between NSW hospital peer groups for VTE mortality, nor did other studies for FTR rates.[45 46 67] However, we did observe greater variation in VTE mortality within peer groups comprising smaller sized hospitals in comparison to larger principal referral hospitals.

Our study showed a significant performance difference between hospitals, within each hospital peer group, with the highest and those with the lowest VTE incidence and associated mortality. Similarly, the association between the two outcomes also varied across groups. Smaller hospitals (district groups 1 and 2) exhibited larger differences in both outcomes, suggesting a greater variability of patient care practice and outcomes amongst this group of hospitals and the greater potential for intervention aimed at VTE prevention and treatment for this group. We also noted a positive association between VTE incidence and VTE mortality amongst smaller size hospital groups. In contrast, larger NSW hospitals tended to have ~~had~~ a higher VTE incidence but lower VTE associated mortality, suggests that there may be a volume-outcome relationship or a greater adherence to evidence-based prevention and treatment guidelines that may explain this better VTE associated mortality. Interestingly, if the higher incidence of VTE alone was used as a measure of failure-to-prevent, these hospitals may be considered to have performed poorly overall, despite the better VTE associated mortality. Conversely, if the higher incidence rates of VTE were largely due to patient selection and case-mix, these hospitals could be considered as better quality hospitals having a lower failure-to-rescue rate with better treatment outcomes. Further investigation into the factors that may explain these differences and the ideal reporting measures is warranted.

Our study raised several important policy implications. Firstly, despite the fact that national and state agencies had developed evidence-based guidelines, such as the Clinical Excellence Commission of NSW "Medication Safety",[65] in which VTE prevention practices were promoted and related incidents evaluated, the increasing incidence of VTE and unchanged VTE mortality question the effectiveness of current national policy and local programs in reducing VTE incidence and mortality. Secondly, the development of systematic local program based on relevant international experience in successfully reducing VTE rate and its related mortality needs urgent policy action. Thirdly, the large variability of VTE rate and its related mortality between and within different hospital peer groups suggests that there is room for improvement in both the prevention and treatment of VTE and that VTE still remains a preventable complication. Lastly, as an important indicator of the quality of care, the level of standardised reporting of VTE in Australia should be explored.

The strengths of our study are that it is the first population-based observational study across all acute public hospitals within the one (i.e. NSW) health region. We used a standardised measure and presented both incidence rates of VTE and VTE associated mortality, thus enabling to differentiate between the two outcome measures and allow for international comparisons. Limitations of our study include that we specifically studied only elective surgical patients according to AHRQ definitions; whereas the analyses of all patient populations may provide addition insight. Future research needs to provide more evidence on the whole inpatient population. We also may have under-reported our findings because of possible coding discrepancies. Nevertheless, this study reinforced the importance of developing measures for combating post-operative VTE, and the continual monitoring and public reporting VTE incidence and mortality.[2 66]

CONCLUSION

The significant increase in VTE incidence among surgical patients over an eight-year period, and persisting level of VTE associated mortality, highlights the need for urgent policy interventions. The significant variation for both outcomes between, and within, different hospital peer groups suggests room for improvement in both the prevention and treatment of VTE. Routine measurement and disclosure of both VTE incidence and associated mortality can provide policy-makers, clinicians and researchers with opportunities to monitor and adjust for performance.

CONTRIBUTORS

Conceived and designed the study: HA, JC, AF, and KH. Prepared the data and performed the analyses: HA, JC, and LO. Wrote the paper: HA, JC, SH, AF, and KH.

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COMPETING INTERESTS

Authors had no conflict of interest.

PROVENANCE AND PEER REVIEW

Not commissioned; externally peer reviewed.

DATA SHARING STATEMENT

No additional data are available.

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APPENDIX

1. Procedure codes from ICD-10-AM for selected surgical procedures

Procedure category	Code			
Abdominal aortic aneurysm	33112-00 33115-00 33118-00 33121-00	33151-00 33157-00 33154-00 33160-00		
Coronary artery bypass graft	38497-00 38497-01 38497-02 38497-03 38497-04 38497-05 38497-06 38497-07	38500-00 38500-01 38500-02 38500-03 38500-04 38503-00	38503-01 38503-02 38503-03 38503-04	90201-00 90201-01 90201-02 90201-03
Cholecystectomy	30443-00 30445-00 30446-00 30448-00 30449-00	30454-01 30455-00		
Total hip replacement	49318-00 49319-00 49324-00 49327-00	49330-00 49333-00 49345-00		
Total knee replacement	49518-00 49519-00 49521-00 49521-01 49521-02 49521-03 49524-00 49524-01	49527-00 49534-00 49530-00 49530-01 49533-00 49554-00		

2. Patient mix over the study period.

Characteristic	Year								Total
	2002	2003	2004	2005	2006	2007	2008	2009	
Age (mean, IQ)	55.77 (40-72)	55.87 (40-72)	56.05 (40-72)	56.40 (40-73)	57.23 (41-74)	57.70 (42-74)	57.97 (43-74)	58.54 (44-74)	57.[illegible] (41[illegible]
Charlson index (mean, IQ)	0.66 (0-2)	0.69 (0-2)	0.72 (0-2)	0.73 (0-2)	0.71 (0-2)	0.70 (0-2)	0.49 (0-0)	0.32 (0-0)	0.6[illegible] (0-
Surgery (n, %)									
AAA repair	269 (0.06)	272 (0.06)	252 (0.05)	241 (0.05)	208 (0.04)	199 (0.03)	173 (0.03)	130 (0.02)	[illegible] (0.[illegible]
CABG	1523 (0.35)	1588 (0.36)	1369 (0.30)	1220 (0.24)	1299 (0.24)	1220 (0.21)	1228 (0.20)	1082 (0.17)	[illegible] (0.[illegible]
Cholecystectomy	6083 (1.41)	6235 (1.42)	5971 (1.29)	6202 (1.22)	6687 (1.21)	6426 (1.09)	6560 (1.08)	5981 (0.94)	[illegible] (1.[illegible]
Hip replacement	2079 (0.48)	2113 (0.48)	2129 (0.46)	2415 (0.48)	2415 (0.44)	2375 (0.40)	2623 (0.43)	2622 (0.41)	[illegible] (0.[illegible]
Knee replacement	3019 (0.70)	2954 (0.67)	3043 (0.66)	3970 (0.78)	4297 (0.78)	4026 (0.68)	4106 (0.68)	4013 (0.63)	[illegible] (0.[illegible]
Other	418211 (96.99)	424896 (97.00)	449687 (97.24)	494049 (97.24)	535782 (97.29)	577727 (97.59)	592941 (97.58)	619407 (97.82)	4114[illegible] (97.[illegible]

IQ: Interquartile; CABG: Coronary Artery Bypass Graft; AAA repair: Abdominal Aortic Aneurysm repair.

FIGURE LEGENDS

Figure 1. Adjusted trends of post-operative VTE and post-VTE death incidence rates (per 1000 elective surgical patients, and 1000 patients with post-operative VTE respectively) over the study period. Rates were estimated by multiplying incidence rate ratio (obtained from the Poisson mix model) and crude risk at the reference year (2002).

Figure 2. Hospital peer group-specific adjusted trends of post-operative VTE (left panel) and post-VTE death (right panel) incidence rates (per 1000 elective surgical patients, and 1000 patients with post-operative VTE respectively) over the study period. Rates were estimated by multiplying incidence rate ratio (obtained from the Poisson mix model including an interaction term for "hospital peer group × year") and crude risk of the reference hospital group (Principal referral) at the reference year (2002).

Figure 3. Surgical procedure-specific adjusted trends of post-operative VTE incidence rates (per 1000 elective surgical patients) over the study period. Rates were estimated by multiplying incidence rate ratio (obtained from the Poisson mix model including an interaction term for "surgery type × year") and crude risk of the reference surgery group (AAA repair) at the reference year (2002).

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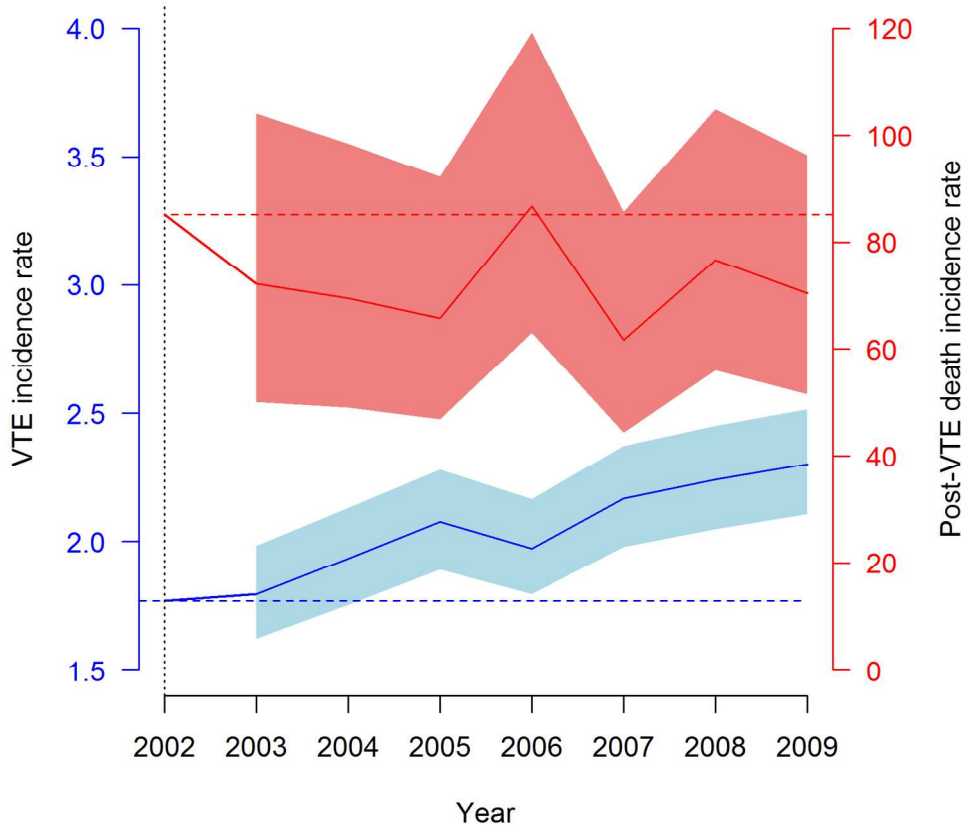

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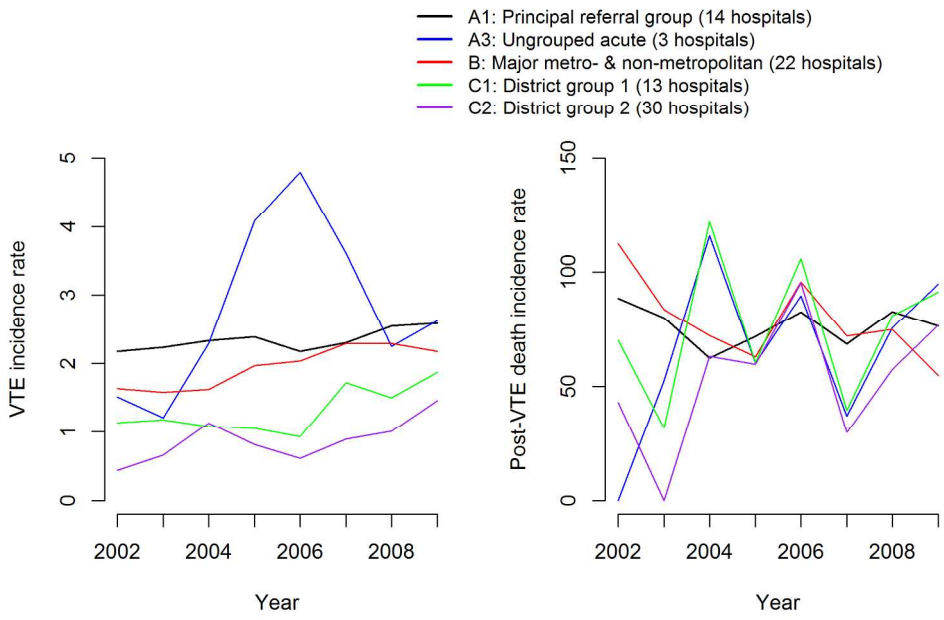

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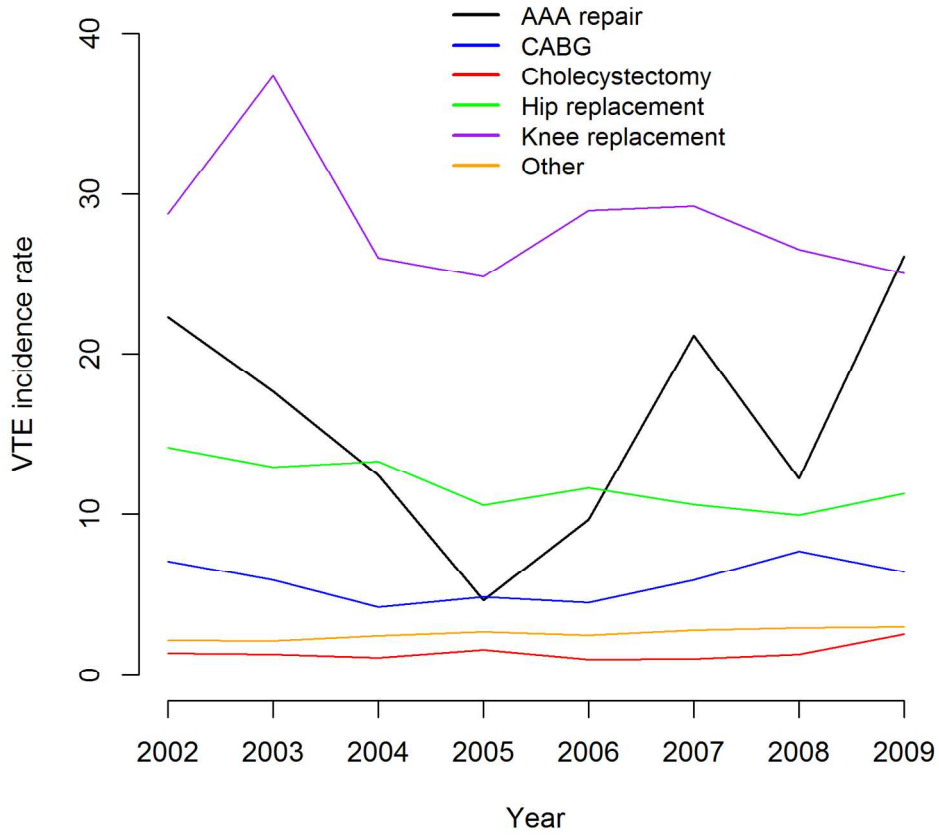

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Coronary artery bypass graft	38497-00	38500-00	38503-01	90201-00
	38497-01	38500-01	38503-02	90201-01
	38497-02	38500-02	38503-03	90201-02
	38497-03	38500-03	38503-04	90201-03
	38497-04	38500-04		
	38497-05	38503-00		
	38497-06			
	38497-07			
Cholecystectomy	30443-00	30454-01		
	30445-00	30455-00		
	30446-00			
	30448-00			
	30449-00			
Total hip replacement	49318-00	49330-00		
	49319-00	49333-00		
	49324-00	49345-00		
	49327-00			
Total knee replacement	49518-00	49527-00		
	49519-00	49534-00		
	49521-00	49530-00		
	49521-01	49530-01		
	49521-02	49533-00		
	49521-03	49554-00		
	49524-00			
	49524-01			

2. Patient mix over the study period.

Characteristic	Year								Total
	2002	2003	2004	2005	2006	2007	2008	2009	
Age (mean, IQ)	55.77 (40-72)	55.87 (40-72)	56.05 (40-72)	56.40 (40-73)	57.23 (41-74)	57.70 (42-74)	57.97 (43-74)	58.54 (44-74)	55.77 (41-73)
Charlson index (mean, IQ)	0.66 (0-2)	0.69 (0-2)	0.72 (0-2)	0.73 (0-2)	0.71 (0-2)	0.70 (0-2)	0.49 (0-0)	0.32 (0-0)	0.61 (0-1)
Surgery (n, %)									
AAA repair	269 (0.06)	272 (0.06)	252 (0.05)	241 (0.05)	208 (0.04)	199 (0.03)	173 (0.03)	130 (0.02)	1744 (0.04)
CABG	1523 (0.35)	1588 (0.36)	1369 (0.30)	1220 (0.24)	1299 (0.24)	1220 (0.21)	1228 (0.20)	1082 (0.17)	10529 (0.25)
Cholecystectomy	6083 (1.41)	6235 (1.42)	5971 (1.29)	6202 (1.22)	6687 (1.21)	6426 (1.09)	6560 (1.08)	5981 (0.94)	50145 (1.19)
Hip replacement	2079 (0.48)	2113 (0.48)	2129 (0.46)	2415 (0.48)	2415 (0.44)	2375 (0.40)	2623 (0.43)	2622 (0.41)	18771 (0.44)
Knee replacement	3019 (0.70)	2954 (0.67)	3043 (0.66)	3970 (0.78)	4297 (0.78)	4026 (0.68)	4106 (0.68)	4013 (0.63)	29428 (0.70)
Other	418211 (96.99)	424896 (97.00)	449687 (97.24)	494049 (97.24)	535782 (97.29)	577727 (97.59)	592941 (97.58)	619407 (97.82)	4112700 (97.38)

IQ: Interquartile; CABG: Coronary Artery Bypass Graft; AAA repair: Abdominal Aortic Aneurysm repair.

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any pre-specified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5-6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	5
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-6
Bias	9	Describe any efforts to address potential sources of bias	6
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5-6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	6
		(*c*) Explain how missing data were addressed	6 , 8-Table 1
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	NA

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	6 (partly)
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8-Table 1
		(b) Indicate number of participants with missing data for each variable of interest	NA
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	NA
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	NA
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	NA
		Cross-sectional study—Report numbers of outcome events or summary measures	8-Table 1
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6-10(Tables 1 & T)
		(*b*) Report category boundaries when continuous variables were categorized	5, 8-10(Tables 1 & T)
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7, Figure 2
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11, 12 , 14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11-14
Generalisability	21	Discuss the generalisability (external validity) of the study results	11, 12, 14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Rate of venous thromboembolism among surgical patients in Australian hospitals: A multicentre retrospective cohort study

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Manuscript ID:	bmjopen-2014-005502.R2
Article Type:	Research
Date Submitted by the Author:	25-Aug-2014
Complete List of Authors:	Assareh, Hassan; University of New South Wales, Simpson Centre for Health Services Research Chen, Jack; University of New South Wales, Simpson Centre for Health Services Research Ou, Lixin; University of New South Wales, Simpson Centre for Health Services Research Hollis, Stephanie; University of New South Wales, Simpson Centre for Health Services Research Hillman, Ken; University of New South Wales, Simpson Centre for Health Services Research Flabouris, Arthas; University of Adelaide, Royal Adelaide Hospital
Primary Subject Heading:	Health services research
Secondary Subject Heading:	Epidemiology, Haematology (incl blood transfusion), Surgery
Keywords:	Patient Safety, Post-operative Complication, Public Hospital, Quality Improvement, Venous Thromboembolism

Title: Rate of venous thromboembolism among surgical patients in Australian hospitals: A multicentre retrospective cohort study

Running title: Post-operative venous thromboembolism in Australia

Authors: Hassan Assareh [*], Jack Chen [*], Lixin Ou [*], Stephanie J. Hollis [*], Kenneth Hillman [*], Arthas Flabouris †

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Keywords: Patient Safety, Post-operative Complication, Public Hospital, Quality Improvement, Venous Thromboembolism.

Word count: Main text: 3450 Abstract: 300 Article summary: 181

Rate of Venous Thromboembolism among Surgical Patients in Australian Hospitals: A Multicentre Retrospective Cohort Study

ABSTRACT

Objectives: Despite the burden of venous thromboembolism (VTE) among surgical patients on health systems in Australia, data on VTE incidence and its variation within Australia is lacking. We aim to explore VTE incidence and associated mortality rates, and their trends and variations across Australian acute public hospitals.

Setting: A large retrospective cohort study using all elective surgical patients in 82 acute public hospitals during 2002-2009 in New South Wales, Australia.

Participants: Patients who had elective surgery within two days of admission, aged between 18 – 90 years, and were not transferred to another acute care facility; 4,362,624 patients were included.

Outcome Measures: VTE incidents were identified by secondary diagnostic codes. Poisson mixed models were used to derive adjusted incidence rates and rate ratios (IRR) in presence of patient and hospital characteristics.

Results: Two per 1000 patients developed post-operative VTE. VTE increased by 30% (IRR=1.30, CI: 1.19-1.42) over the study period. Differences in the VTE rates, trends between hospital peer groups and between hospitals with the highest and those with the lowest rates were significant (between-hospital variation). Smaller hospitals, accommodated in two peer groups, had the lowest overall VTE rates (IRR=0.56:0.33-0.95; IRR=0.37:0.23-0.61) and exhibited a greater increase (64% and 237% vs. 19%) over time and greater between-hospital variations compared to larger hospitals (IRR=8.64:6.23-11.98; IRR=8.92:5.49-14.49 vs. IRR=3.70:3.32-4.12). Mortality among patients with post-operative VTE was 8% and remained stable over time (IRR=0.98:0.95-1.02). No differences in post-VTE death rates and trends were seen between hospital groups; however larger hospitals exhibited less between-hospital variations (IRR=1.78:1.30-2.44) compared to small hospitals (IRR>23). Hospitals performed differently in prevention versus treatment of post-operative VTE.

Conclusions: The incidence of VTE is increasing and there is large variation between- and within-hospital peer groups suggesting a varied compliance with VTE preventative strategies and the potential for targeted interventions and quality improvement opportunities.

ARTICLE SUMMARY

Article focus

- To evaluate rates and trends of post-operative VTE incidence and subsequent mortality within Australian hospitals
- To demonstrate and compare variations of VTE incidence and subsequent deaths between hospitals

Key messages

- Post-operative VTE incidence rate was two per 1000 patients. It increased by 28% over the study period. Post-VTE mortality rate was 8% and remained stable over time.
- Smaller hospitals had lower VTE rates but exhibited a greater increase over time and greater between-hospital variations compared to larger hospitals. They also exhibited greater between-hospital variations in post-VTE death rates.

Strengths and limitations of this study

- This study benefited from a large cohort design within the largest health jurisdiction in Australia.
- Employment of standardised and broadly-applied VTE measures facilitated local and international comparisons and benchmarking.
- Demonstration of trends and variations in VTE measures reflected effectiveness of systematic interventions and revealed opportunities for further improvement and actions at local and regional levels.
- This study was limited to VTE incidence among elective surgical patients. Analysis of all patient populations may provide addition insight.
- The obtained rates may have under-estimated due to possible coding discrepancies.

INTRODUCTION

Venous thromboembolism (VTE), comprised of deep-vein thrombosis (DVT) and pulmonary embolism (PE), can cause long-term comorbidities or death[1 2] and incur significant financial burden on healthcare systems.[3 4] It accounts for nearly 10% of all deaths in U.S. [5 6] and Australian hospitals,[7 8] and is amongst the top five most common causes of hospital-related deaths in both countries.[3 9] However, VTE is also the most common preventable cause of hospital deaths.[10-13] A significant decrease in VTE incidents has been reported where efficacious and cost-effective treatments (ie. pharmacological and mechanical prophylaxis) were used for both medical and surgical patients.[1 12 14-19] Accordingly, several evidence-based VTE prevention and treatment guidelines were developed[1 9 20] and related measures were adopted among quality of care indices for accreditation, quality improvement and benchmarking purposes.[21-23]

The Agency for Healthcare Research and Quality (AHRQ) listed post-operative VTE complications (VTE incidence following surgery) and subsequent death as a component of failure-to-rescue (FTR) among patient saftey indicators (PSI#12 and PSI#4-2 respectively), which are routinely being monitored and publically reported.[23 24] Reports showed that the post-operative VTE incidence rates have nearly halved in U.S. hospitals in recent years,[24 25] and post-VTE mortality rate declined by a third within a decade since the mid-90s.[26] These rate decreases may be, in part, due to the implementation of post-operative VTE prevention protocols,[27] however substantial variation in post-operative VTE incidence rate was also evident among U.S. hospitals.[25] Although patients case mix and surgery types may play a role in such differences,[6 28 29] the variation of VTE incidence among the same type of hospitals over time and within the group may reflect the success of quality improvement interventions and demonstrate the potential for further development.[30 31]

Few Australian studies have reported VTE incidence,[3 8 32] and the measures of VTE used in these studies varied making comparison difficult. Consequently, we employed the internationally-recognised AHRQ measures for post-operative VTE, and subsequent mortality, to explore the trend of the incidence rates and their variations among admitted surgical patients in acute public hospitals across New South Wales (NSW), Australia (2002-2009).

METHODS

Data source and study population

New South Wales is the largest health jurisdiction in Australia with approximately 497 healthcare facilities and a population of over seven million people. We used records from the NSW Admitted

Patient Data Collection (APDC) database, which includes all admitted patient services provided by NSW public and private healthcare facilities. The APDC includes information on patient demographics, medical conditions and procedures, hospital characteristics, and separations (discharges, transfers and deaths) from all public and private hospitals (as well as day procedure centres) in NSW. The medical records for each episode of care in the APDC were assigned with codes based on the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification (ICD-10-AM) 4th edition.[33] Of admissions at 497 healthcare facilities across NSW between 1st January 2002 to 31st December 2009, we included all 82 NSW acute public hospitals (9,221,128 admissions; 57.4%) in our study. Two children's hospitals and one other hospital (data was unavailable) were excluded We restricted our study to only elective surgical patients and applied the same AHRQ inclusion criteria[23] for patients who had elective surgery within two days of admission, aged between 18 – 90 years (inclusive), and were not transferred to another acute care facility (4,362,624 episodes (47.3%)). Ethical approval was obtained from the University of NSW Human Research Ethics Committee (LNR/11/CIPHS/64).

Measures and covariates

Of surgical patients who met AHRQ inclusion criteria (patients at risk), those who developed VTE were identified by secondary diagnostic codes (ICD-10-AM) translated from the AHRQ definition (ICD-9-CM) by Victorian Government Health Information.[34] The outcome measure was teremed "post-operative VTE", proposed by the Australian version of patient safety indicators (AusPSI),[35] instead of "peri-operative VTE" term suggested by AHRQ.[23] We used "post-operative VTE" term since employment of inclusing criteria (undergoing surgery within two days of admission and secondary diagnosis of VTE) miminmised likelihood of VTE presence on admission or VTE occurance prior surgery. In combination with discharge status, patients post-VTE outcomes were categorised as survival or death. VTE and related death rates were presented as incidences per 1000 admissions within each year between 2002 and 2009, inclusively.

Two sets of patient- and hospital-related covariates were considered. Patient demographic variables included age, gender, country of birth, marital status, patient socio-economic status, and principle diagnostic disease groups (the ten most common) within the study population. We utilised a postcode-level advantage and disadvantage index of Socio-Economic Indices for Areas (SEIFA) with the lower values indicating more disadvantaged areas.[36] SEIFA scores were categorised into four classes (1st quartile = most disadvantaged areas and 4th quartile = most advantaged areas). The disease groups were identified using principle diagnostic codes (ICD-10-AM) at admissions through the methodology develop by Quan et al..[37] Using relevant procedure codes from ICD-10-AM

(Appendix 1), we defined six major surgical procedures including coronary-artery bypass graft (CABG), abdominal aortic aneurysm (AAA) repair, total hip replacement, total knee replacement, cholecystectomy, and other surgical procedures.

Hospital covariates included the local health district (metropolitan, rural and regional NSW) and peer group (A1: principal referral group, usually teaching hospitals; A3: ungrouped acute; B: major metropolitan and non-metropolitan; C1: district group 1; and, C2: district group 2). Hospital peer groups contained similar type and sized hospitals, ranging from those treating more than 25,000 acute case-mix weighted separations per annum in principal referral groups through to treating 2,000^{+} (but less than 5,000) acute case-mix weighted separations per annum in district group 2.[38]

Statistical analysis

We employed Poisson mixed models to evaluate adjusted incidence rates and rate ratios for study outcomes after including all patients and hospital-related characteristics. A random intercept term was utilised to incorporate any clustering effect at hospital-level. To investigate the temporal behaviour of the outcomes, calendar years were entered into the model as indicator variables, with 2002 as the reference year. A model with the year as a continuous variable was also examined for linear trends. We derived hospital peer group and surgery type trends using interaction effects (year and hospital peer group; year and surgery type) in separate models. Adjusted incidence rates for specific years were derived by multiplying yearly-adjusted risk ratios to the crude risks observed in the reference year.

We initially examined the Elixhauser and the Charlson Index comorbidities based on the ICD-10 coding scheme,[37] however we did not include either of them in the models given an unexpected drop in the comorbidity index among our study population in recent years (Appendix 2) and also recent reports that these indices may introduce misleading results possibly due to geographical variations and biases in the coding.[39-41] To study the variation of outcomes across hospitals within each hospital group, hospital-specific random intercept components were extracted from Poisson mixed models constructed for each hospital group, then ranked and categorised into five classes at 20% incremental quintiles. To obtain adjusted differences between those with the highest and those with the lowest VTE incidence, the adjusted classes were entered into a Poisson model including patient characteristics covariates. We used Pearson correlation to assess the association of hospital performances between VTE and post-VTE deaths, based on the hospital-specific random intercepts. All analyses were performed in R package version 3.0.0[42] and Stata^{TM} 11.0.[43]

RESULT

Table 1 summarised the study population by outcomes across hospital and patient characteristics and related statistics. Of the 4,223,317 (45.8% of all admissions with no missing information) elective surgical admissions during 2002-2009 with a median length of stay of one day (the first (Q1) and the third quartiles (Q3) equal to one day), 8,451 patients developed either DVT or PE after surgery, resulting in an incidence rate of 2 per 1000 surgical patients with a median length of stay of 11 days (Q1=6 and Q3=21days). Among them, 673 (8%) died prior to discharge with a median length of stay of 11 days (Q1=4 and Q3=22 days); 79.6 per 1000 patients with post-operative VTE. Compared to females, males tended to have a lower risk of post-operative VTE (IRR=0.91); however, they were more likely to die (IRR=1.19) following a VTE. Older patients were exposed to higher risks of VTE and death after surgery. Married patients and those who were born in Europe (except the UK), Asia and North Africa experienced a lower risk of post-operative VTE compared to their counterparts but a similar risk of post-VTE death.

Patients admitted with malignancy and congestive heart failure had the highest VTE and hospital mortality rates. Patients who underwent total knee replacement, AAA repair and total hip replacement surgeries had higher risk of VTE, respectively; however, post-VTE mortality was lower among orthopaedic surgical patients compared to other procedures. Higher socio-economic status (quartiles of SEIFA) of patients was associated with a lower risk of VTE. There was no difference in mortality for patients residing in advantaged and disadvantaged areas. Patients from principal referral hospitals were more likely to acquire VTE in comparison to the patients from district hospitals (IRR= 0.56 and 0.37 for group 1 and 2 hospitals respectively). No differences in outcomes were observed between metropolitan and non-metropolitan hospitals.

Post-operative VTE incidence rate significantly increased over the study period by 30%, from 1.77 per 1000 patients in 2002 to 2.30 in 2009 (Figure 1). Despite some fluctuation, all hospital peer groups exhibited similar increasing trends in post-operative VTE incidence over the study period after adjustment for patient demographics (Figure 2), ranging from 19% (2.58 vs. 2.17) in principal referral hospitals to 237% (1.21 vs. 0.36) in district group 2. Surgery-specific VTE rates for the five procedures exhibited high fluctuations and insignificant trends, whereas the other surgery group showed a steady increasing trend of 38% (3.01 vs. 2.18) over the study period (Figure 3). Post-VTE mortality fluctuated between 68 to 97 cases per 1000 patients over the study period with no significant change after adjusting for confounders overall (Figure 1) and at hospital peer group level (Figure 2). Mortality tended to be stable across hospital peer groups as between-group variation of mortality

reduced over the study period. No surgery-specific trend analysis was conducted due to small number of post-DVT deaths per annum.

The incidence rate ratios between those hospitals with the lowest, and those with the highest rate, was larger in VTE related mortality than in VTE and varied across hospital peer group (Table 2). For VTE, the difference in rate is less than four-fold in the principal referral and major peer groups (include large hospitals) but at least eight-fold in district peer groups (include small hospitals). Similarly, the difference in rate is larger in district group 1 and 2 (IRR=23 and 38) compared to principal referral (IRR=1.7) and major metropolitan/non-metropolitan hospitals (IRR=15) for VTE related deaths. The close to significant negative correlation (-0.45, P-value=0.057) for principal referral hospitals implied that hospitals with the highest post-operative VTE rate tended to have a lower rate of subsequent death. In contrast, within district group 2 (0.41), hospitals with higher VTE rates tended to also have the highest post-VTE death rates. There were no such associations within other peer groups.

Table 1. Study population, incidence rates (IR) and adjusted incidence rate ratios (IRR) of surgical patients who developed VTE and died, stratified by patient and hospital characteristics.

Characteristics	Surgical patients n (%)	VTE			VTE associated death		
		Frequency (%)	IR	IRR (95% CI)	Frequency (%)	IR	IRR (95% CI)
Sex							
Female	2280384 (54.00)	4626 (54.74)	2.03	1.00	330 (49.03)	71.34	1.00
Male	1942933 (46.00)	3825 (45.26)	1.97	0.90 (0.86-0.94) **	343 (50.97)	89.67	1.19 (1.02-1.40) *
Age							
>=18yr & <35yr	738382 (17.48)	487 (5.76)	0.66	0.21 (0.19-0.23) **	11 (1.63)	22.59	0.20 (0.11-0.37) **
>=35yr & <55yr	1013921 (24.01)	1308 (15.48)	1.29	0.42 (0.40-0.45) **	82 (12.18)	62.69	0.58 (0.45-0.74) **
>=55yr & <75yr	1595024 (37.77)	3538 (41.86)	2.22	0.66 (0.63-0.70) **	290 (43.09)	81.97	0.85 (0.72-1.01)
>=75yr & <90	875990 (20.74)	3118 (36.90)	3.56	1.00	290 (43.09)	93.01	1.00
Marital status							
Married	2548508 (60.34)	4667 (55.22)	1.83	1.00	381 (56.61)	81.64	1.00
Single	1674809 (39.66)	3784 (44.78)	2.26	1.16 (1.11-1.21) **	292 (43.39)	77.17	1.01 (0.86-1.18)
Country of birth							
Australia and New Zealand	2839135 (67.23)	5858 (69.32)	2.06	1.00	479 (71.17)	81.77	1.00
UK, US & Canada	239088 (5.66)	645 (7.63)	2.70	1.06 (0.97-1.15)	53 (7.88)	82.17	0.95 (0.72-1.27)
Non-English Europe	447239 (10.59)	1046 (12.38)	2.34	0.74 (0.69-0.80) **	80 (11.89)	76.48	0.91 (0.71-1.16)
North Africa	130938 (3.10)	139 (1.64)	1.06	0.47 (0.40-0.56) **	9 (1.34)	64.75	0.87 (0.45-1.70)
Asia	179725 (4.26)	193 (2.28)	1.07	0.45 (0.39-0.52) **	16 (2.38)	82.90	1.09 (0.66-1.80)
Others	387192 (9.17)	570 (6.74)	1.47	0.58 (0.53-0.64) **	36 (5.35)	63.16	0.95 (0.67-1.35)
Major surgical procedure							
AAA repair	1744 (0.04)	26 (0.31)	14.91	1.00	6 (0.89)	230.77	1.00
CABG	10529 (0.25)	52 (0.62)	4.94	0.37 (0.23-0.60) **	7 (1.04)	134.62	0.69 (0.23-2.10)
Cholecystectomy	50145 (1.19)	42 (0.50)	0.84	0.09 (0.05-0.15) **	6 (0.89)	142.86	0.70 (0.22-2.22)
Total hip replacement	18771 (0.44)	207 (2.45)	11.03	0.74 (0.49-1.11)	4 (0.59)	19.32	0.12 (0.03-0.44) **
Total knee replacement	29428 (0.70)	798 (9.44)	27.12	1.76 (1.19-2.61) **	3 (0.45)	3.76	0.03 (0.01-0.11) **
Other	4112700 (97.38)	7326 (86.69)	1.78	0.17 (0.11-0.24) **	647 (96.14)	88.32	0.52 (0.23-1.19)
Major principle diagnostic diseases†							
Cardiac arrhythmias	25953 (0.61)	75 (0.89)	2.89	-	2 (0.30)	26.67	-
Chronic pulmonary disease	11558 (0.27)	69 (0.82)	5.97	-	6 (0.89)	86.96	-
Coagulopathy	3908 (0.09)	37 (0.44)	9.47	-	2 (0.30)	54.05	-
Congestive heart failure	6765 (0.16)	85 (1.01)	12.56	-	17 (2.53)	200.00	-
Diabetes with chronic complication	33541 (0.79)	79 (0.93)	2.36	-	11 (1.63)	139.24	-

Malignancy including lymphoma & leukaemia	150962 (3.57)	1070 (12.66)	7.09	-		182 (27.04)	170.09	-
Metastatic solid tumour	19699 (0.47)	291 (3.44)	14.77	-		67 (9.96)	230.24	-
Peripheral vascular disease	15993 (0.38)	141 (1.67)	8.82	-		10 (1.49)	70.92	-
Renal failure	1385753 (32.81)	42 (0.50)	0.03	-		1 (0.15)	23.81	-
Rheumatoid arthritis/collagen vascular disease	10748 (0.25)	40 (0.47)	3.72	-		1 (0.15)	25.00	-
Year								
2002	431184 (10.21)	763 (9.03)	1.77	1.00		65 (9.66)	85.19	1.00
2003	438058 (10.37)	780 (9.23)	1.78	1.01 (0.92-1.12)		53 (7.88)	67.95	0.85 (0.59-1.22)
2004	462451 (10.95)	878 (10.39)	1.90	1.09 (0.99-1.20)		65 (9.66)	74.03	0.82 (0.58-1.16)
2005	508097 (12.03)	1038 (12.28)	2.04	1.17 (1.07-1.29)	**	75 (11.14)	72.25	0.77 (0.55-1.08)
2006	550688 (13.04)	1062 (12.57)	1.93	1.11 (1.01-1.22)	*	103 (15.30)	96.99	1.02 (0.74-1.40)
2007	591973 (14.02)	1223 (14.47)	2.07	1.22 (1.12-1.34)	**	87 (12.93)	71.14	0.72 (0.52-1.01)
2008	607631 (14.39)	1313 (15.54)	2.16	1.27 (1.16-1.38)	**	112 (16.64)	85.30	0.90 (0.66-1.23)
2009	633235 (14.99)	1394 (16.50)	2.20	1.30 (1.19-1.42)	**	113 (16.79)	81.06	0.83 (0.60-1.13)
Year-linear trend	-	-	-	1.04 (1.03-1.05)	**	-	-	0.98 (0.95-1.02)
Quartiles of SEIFA								
1st quartile (most disadvantaged)	1089833 (25.81)	2308 (27.31)	2.12	1.00		187 (27.79)	81.02	1.00
2nd quartile	1084727 (25.68)	1981 (23.44)	1.83	0.88 (0.82-0.94)	**	169 (25.11)	85.31	0.96 (0.78-1.20)
3rd quartile	1074283 (25.44)	2088 (24.71)	1.94	0.76 (0.72-0.81)	**	175 (26.00)	83.81	1.04 (0.84-1.30)
4th quartile (most advantaged)	974474 (23.07)	2074 (24.54)	2.13	0.70 (0.65-0.75)	**	142 (21.10)	68.47	0.98 (0.77-1.26)
Peer hospital groups								
Principal referral	2269392 (53.73)	5141 (60.83)	2.27	1.00		381 (56.61)	74.11	1.00
Ungrouped acute	133465 (3.16)	380 (4.50)	2.85	1.20 (0.54-2.66)		43 (6.39)	113.16	0.94 (0.37-2.39)
Major metro- & non-metropolitan	1140036 (26.99)	2125 (25.14)	1.86	0.84 (0.54-1.31)		183 (27.19)	86.12	0.96 (0.60-1.55)
District group 1	346910 (8.21)	484 (5.73)	1.40	0.56 (0.33-0.95)	*	42 (6.24)	86.78	0.99 (0.54-1.83)
District group 2	333514 (7.90)	321 (3.80)	0.96	0.37 (0.23-0.61)	**	24 (3.57)	74.77	0.74 (0.38-1.44)
Local health district								
Metropolitan	2720690 (64.42)	5882 (69.60)	2.16	1.00		430 (63.89)	73.10	1.00
Rural & Regional NSW	1502627 (35.58)	2569 (30.40)	1.71	0.74 (0.52-1.05)		243 (36.11)	94.59	1.26 (0.82-1.92)
Total	4223317	8451	2.00	-		673	79.64	-

139,307 (3.2%) cases were excluded due to missing or unknown items.
Incidence rates (IR) are crude and reported per 1000 patients.
Risk ratios (RR) and related confident intervals (CI) were obtained using a Poisson mixed model.
CABG: Coronary Artery Bypass Graft; AAA repair: Abdominal Aortic Aneurysm repair.
† No RR is reported since this characteristic has not been included in the Poisson mixed model.
* Significant at 5%; ** significant at 1%.

Table 2. Incidence rates (IR), adjusted incidence rate ratios (IRR) and association of outcomes between the best and worst performers (top and bottom 20% quintiles) within hospital peer groups

Hospital peer group	Hospital n	VTE				Post-VTE death				Correlation coefficient (95% CI)	
		Lowest (IR)	Highest (IR)	IRR (95% CI)		Lowest (IR)	Highest (IR)	IRR (95% CI)			
Principal referral	17	1.24	4.00	3.70 (3.32-4.12)	**	43.58	131.12	1.78 (1.30-2.44)	**	-0.45 (-0.79, 0.01)	
Major metro- & non-metropolitan	22	1.00	2.99	3.85 (3.33-4.46)	**	16.80	162.30	15.48 (6.45-37.12)	**	0.15 (-0.28,0.54)	
District group 1	13	0.42	3.71	8.64 (6.23-11.98)	**	13.88	242.71	38.02 (10.25-140.94)	**	-0.37 (-0.76,0.22)	
District group 2	30	0.22	2.15	8.92 (5.49-14.49)	**	16.66	104.97	23.26 (2.94-183.50)	**	0.41 (0.05,0.68)	*

Incidence rates (IR) are crude and reported per 1000 patients.
Risk ratios (RR) and related confident intervals (CI) were obtained using a Poisson model and adjusted for patient characteristics. Those hospitals with the lowest rate were set as the reference level.
Ungrouped acute group was removed from analysis due to small number of hospitals within this group.
* Significant at 5%; ** significant at 1%.

DISCUSSION

In this large cohort study, of elective surgical patients, from all NSW acute public hospitals, over an 8 year period, we found that the incidence of VTE to be two of 1000 elective surgical admissions, and VTE associated mortality to be 8%. The adjusted incidence of VTE increased significantly over the study period (30%), with no change in mortality. There were significant differences in incidence of VTE between hospital peer groups and between hospitals with the lowest and those with the highest rate. Principal referral hospitals exhibited a higher overall incidence, but lower intragroup variation compared to other peer groups. Principal referral hospitals with a higher incidence of VTE also tended to have a lower VTE-related mortality.

The incidence of post-operative VTE in NSW hospitals was less than half that of. U.S. hospitals within a similar period (4.5 or more per 1000 patients in 2010 and prior),[25 44] but with a similar VTE associated mortality (83 vs. 79 per 1000 patients). [25] Based upon our findings, VTE incidence and associated mortality contributes to approximately 15% and 8% of overall failure-to-rescue (FTR)-related incidence and mortality (13.8 and 140 per 1000 patients, respectively).[45 46] Despite the fact that our study and the U.S. study used the identical measure defined by AHRQ,[23] the discrepancies and coding practices between the U.S. (ICD-9-CM) and Australia (ICD-10-AM) may, in part, have contributed to the difference. It was shown that accuracy of VTE coding can be improved by the adoption of extended codes developed in the revised ICD-9-CM. [47]

In a recent Organization for Economic and Co-Operation and Development (OECD) report, Australian-wide incidence were 0.97 and 1.26 per 1000 patients in 2009 and 2012 respectively, placing Australia among three nations (Australia, Slovenia and the U.S.) with the highest incidence of approximately one per a thousand surgical patients or more within the last decade.[48] Our observed rate for NSW hospitals was nearly double that of the OCED provided Australian rates, possibly due to the fact that we studied only elective surgical patients from acute public hospitals. Such cross-nations reports provide a platform for health service comparisons and the study of longitudinal variations. However, internal and external comparability of OCED results may be affected by the heterogeneity and biases of the different nation's coding systems.

Despite continued poor compliance with VTE prevention guidelines and VTE preventative measures,[49-52] post-operative VTE incidence in U.S. hospitals almost halved between 2007-2011.[24 44] In Australia, given the overt gap between evidence and practice of VTE prevention protocols,[53 54] the National Institute of Clinical Studies (NICS) launched a VTE prevention program in 85 public and private hospitals across Australia between 2005-2008 which resulted in

increased awareness of and adherence with VTE prevention guidelines.[2 55] However, we found an increasing trend in NSW post-operative VTE incidence rate within 2002-2009, with an approximate 4% annual increase and total increase of 30%, mostly contributed by the higher incidence in the smaller hospital peer groups (237%) compared to the large teaching hospital group (19%). The reason for this increase is unclear.

Our finding of a higher incidence of VTE and VTE associated mortality with increasing age is similar that observed by others.[29 56-58] Ageing previously accepted as a major contributing factor to the increasing trends in VTE rates for admitted patients in Australian hospitals.[3] However, we have taken into account patient characteristics including age as well as surgery type and demonstrated an adjusted increasing trend for surgical patients, despite the observed decreasing trends in proportions of AAA repair and orthopaedic surgical procedures (Appendix 2) known with high post-operative VTE risks (Table 1).[1] Notably, the steadily increasing VTE incidences among patients who underwent other surgical procedures mainly contributed to the observed overall trend (Figure 3). More research is required to examine the contributing factors for such a difference among different surgical procedures. In particular, comorbidity-specific analysis at hospital level is encouraged to minimise potential biases reported elsewhere.[39-41]

Although other studies suggest gender may not be a significant risk factor for VTE,[28 29 59] we found males were less likely to develop VTE complications, but more likely to subsequently die. We did not separately explore DVT and PE incidence and associated deaths between genders; but our higher mortality risk for males can be explained by the estimated higher odds of PE (vs. DVT which has a lower risk of death[29 59] for males compared to females (1.87 vs. 1.02 respectively) in Australian hospitals during our study period.[3]

Variation in the application of VTE prevention guidelines and other quality initiatives may have contributed to the differences in outcomes amongst the hospitals in our study. Smaller, district 1 and 2 peer groups hospitals, had a significantly lower VTE incidence rate compared to larger hospitals in NSW. This was in contrast with other studies which showed that larger hospitals have a lower mortality following major procedures, such as orthopaedic surgeries[60 61] and post-operative complications such as VTE.[62] A possible explanation for this discrepancy is that principal referral hospitals undertook higher risk patients and surgical complexity than the smaller district hospitals. Geographical variations in coding,[39-41] underreporting of VTE due to mis-coding to a more general cardiovascular item,[3 63] and high diagnosis likelihood of high-risk but asymptomatic post-operative patients[64] may also have contributed to elevated VTE rates in major hospitals. We did not observe differences between NSW hospital peer groups for VTE mortality, nor did other studies for

FTR rates. However, we did observe greater variation in VTE mortality within peer groups comprising smaller sized hospitals in comparison to larger principal referral hospitals.

Our study showed a significant performance difference between hospitals, within each hospital peer group, with the highest and those with the lowest VTE incidence and associated mortality. Similarly, the association between the two outcomes also varied across groups. Smaller hospitals (district groups 1 and 2) exhibited larger differences in both outcomes, suggesting a greater variability of patient care practice and outcomes amongst this group of hospitals and the greater potential for intervention aimed at VTE prevention and treatment for this group. We also noted a positive association between VTE incidence and VTE mortality amongst smaller size hospital groups. In contrast, larger NSW hospitals tended to have a higher VTE incidence but lower VTE associated mortality, suggests that there may be a volume-outcome relationship or a greater adherence to evidence-based prevention and treatment guidelines that may explain this better VTE associated mortality. Interestingly, if the higher incidence of VTE alone was used as a measure of failure-to-prevent, these hospitals may be considered to have performed poorly overall, despite the better VTE associated mortality. Conversely, if the higher incidence rates of VTE were largely due to patient selection and case-mix, these hospitals could be considered as better quality hospitals having a lower failure-to-rescue rate with better treatment outcomes. Further investigation into the factors that may explain these differences and the ideal reporting measures is warranted.

Our study raised several important policy implications. Firstly, despite the fact that national and state agencies had developed evidence-based guidelines, such as the Clinical Excellence Commission of NSW "Medication Safety",[65] in which VTE prevention practices were promoted and related incidents evaluated, the increasing incidence of VTE and unchanged VTE mortality question the effectiveness of current national policy and local programs in reducing VTE incidence and mortality. Secondly, the development of systematic local program based on relevant international experience in successfully reducing VTE rate and its related mortality needs urgent policy action. Thirdly, the large variability of VTE rate and its related mortality between and within different hospital peer groups suggests that there is room for improvement in both the prevention and treatment of VTE and that VTE still remains a preventable complication. Lastly, as an important indicator of the quality of care, the level of standardised reporting of VTE in Australia should be explored.

The strengths of our study are that it is the first population-based observational study across all acute public hospitals within the one (i.e. NSW) health region. We used a standardised measure and presented both incidence rates of VTE and VTE associated mortality, thus enabling to differentiate between the two outcome measures and allow for international comparisons. Limitations of our study

include that we specifically studied only elective surgical patients according to AHRQ definitions; whereas the analyses of all patient populations may provide addition insight. Future research needs to provide more evidence on the whole inpatient population. We also may have under-reported our findings because of possible coding discrepancies. Nevertheless, this study reinforced the importance of developing measures for combating post-operative VTE, and the continual monitoring and public reporting VTE incidence and mortality.[2 66]

CONCLUSION

The significant increase in VTE incidence among surgical patients over an eight-year period, and persisting level of VTE associated mortality, highlights the need for urgent policy interventions. The significant variation for both outcomes between, and within, different hospital peer groups suggests room for improvement in both the prevention and treatment of VTE. Routine measurement and disclosure of both VTE incidence and associated mortality can provide policy-makers, clinicians and researchers with opportunities to monitor and adjust for performance.

CONTRIBUTORS

Conceived and designed the study: HA, JC, AF, and KH. Prepared the data and performed the analyses: HA, JC, and LO. Wrote the paper: HA, JC, SH, AF, and KH.

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COMPETING INTERESTS

Authors had no conflict of interest.

PROVENANCE AND PEER REVIEW

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DATA SHARING STATEMENT

No additional data are available.

FIGURE LEGENDS

Figure 1. Adjusted trends of post-operative VTE and post-VTE death incidence rates (per 1000 elective surgical patients, and 1000 patients with post-operative VTE respectively) over the study period. Rates were estimated by multiplying incidence rate ratio (obtained from the Poisson mix model) and crude risk at the reference year (2002).

Figure 2. Hospital peer group-specific adjusted trends of post-operative VTE (left panel) and post-VTE death (right panel) incidence rates (per 1000 elective surgical patients, and 1000 patients with post-operative VTE respectively) over the study period. Rates were estimated by multiplying incidence rate ratio (obtained from the Poisson mix model including an interaction term for "hospital peer group × year") and crude risk of the reference hospital group (Principal referral) at the reference year (2002).

Figure 3. Surgical procedure-specific adjusted trends of post-operative VTE incidence rates (per 1000 elective surgical patients) over the study period. Rates were estimated by multiplying incidence rate ratio (obtained from the Poisson mix model including an interaction term for "surgery type × year") and crude risk of the reference surgery group (AAA repair) at the reference year (2002).

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Title: Rate of venous thromboembolism among surgical patients in Australian hospitals: A ~~large~~ multicentre retrospective cohort study

Running title: Post-operative venous thromboembolism in Australia

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Rate of Venous Thromboembolism among Surgical Patients in Australian Hospitals: A ~~Large~~ Multicentre Retrospective Cohort Study

ABSTRACT

Objectives: Despite the burden of venous thromboembolism (VTE) among surgical patients on health systems in Australia, data on VTE incidence and its variation within Australia is lacking. We aim to explore VTE incidence and associated mortality rates, and their trends and variations across Australian acute public hospitals.

Setting: A large retrospective cohort study using all elective surgical patients in 82 acute public hospitals during 2002-2009 in New South Wales, Australia.

Participants: Patients who had elective surgery within two days of admission, aged between 18 – 90 years, and were not transferred to another acute care facility; 4,362,624 patients were included.

Outcome Measures: VTE incidents were identified by secondary diagnostic codes. Poisson mixed models were used to derive adjusted incidence rates and rate ratios (IRR) in presence of patient and hospital characteristics.

Results: Two per 1000 patients developed post-operative VTE. VTE increased by 30% (IRR=1.30, CI: 1.19-1.42) over the study period. Differences in the VTE rates, trends between hospital peer groups and between hospitals with the highest and those with the lowest rates were significant (between-hospital variation). Smaller hospitals, accommodated in two peer groups, had the lowest overall VTE rates (IRR=0.56:0.33-0.95; IRR=0.37:0.23-0.61) and exhibited a greater increase (64% and 237% vs. 19%) over time and greater between-hospital variations compared to larger hospitals (IRR=8.64:6.23-11.98; IRR=8.92:5.49-14.49 vs. IRR=3.70:3.32-4.12). Mortality among patients with post-operative VTE was 8% and remained stable over time (IRR=0.98:0.95-1.02). No differences in post-VTE death rates and trends were seen between hospital groups; however larger hospitals exhibited less between-hospital variations (IRR=1.78:1.30-2.44) compared to small hospitals (IRR>23). Hospitals performed differently in prevention versus treatment of post-operative VTE.

Conclusions: The incidence of VTE is increasing and there is large variation between- and within-hospital peer groups suggesting a varied compliance with VTE preventative strategies and the potential for targeted interventions and quality improvement opportunities.

ARTICLE SUMMARY

Article focus

- To evaluate rates and trends of post-operative VTE incidence and subsequent mortality within Australian hospitals
- To demonstrate and compare variations of VTE incidence and subsequent deaths between hospitals

Key messages

- Post-operative VTE incidence rate was two per 1000 patients. It increased by 28% over the study period. Post-VTE mortality rate was 8% and remained stable over time.
- Smaller hospitals had lower VTE rates but exhibited a greater increase over time and greater between-hospital variations compared to larger hospitals. They also exhibited greater between-hospital variations in post-VTE death rates.

Strengths and limitations of this study

- This study benefited from a large cohort design within the largest health jurisdiction in Australia.
- Employment of standardised and broadly-applied VTE measures facilitated local and international comparisons and benchmarking.
- Demonstration of trends and variations in VTE measures reflected effectiveness of systematic interventions and revealed opportunities for further improvement and actions at local and regional levels.
- This study was limited to VTE incidence among elective surgical patients. Analysis of all patient populations may provide addition insight.
- The obtained rates may have under-estimated due to possible coding discrepancies.

INTRODUCTION

Venous thromboembolism (VTE), comprised of deep-vein thrombosis (DVT) and pulmonary embolism (PE), can cause long-term comorbidities or death[1 2] and incur significant financial burden on healthcare systems.[3 4] It accounts for nearly 10% of all deaths in U.S. [5 6] and Australian hospitals,[7 8] and is amongst the top five most common causes of hospital-related deaths in both countries.[3 9] However, VTE is also the most common preventable cause of hospital deaths.[10-13] A significant decrease in VTE incidents has been reported where efficacious and cost-effective treatments (ie. pharmacological and mechanical prophylaxis) were used for both medical and surgical patients.[1 12 14-19] Accordingly, several evidence-based VTE prevention and treatment guidelines were developed[1 9 20] and related measures were adopted among quality of care indices for accreditation, quality improvement and benchmarking purposes.[21-23]

The Agency for Healthcare Research and Quality (AHRQ) listed post-operative VTE complications (VTE incidence following surgery) and subsequent death as a component of failure-to-rescue (FTR) among patient saftey indicators (PSI#12 and PSI#4-2 respectively), which are routinely being monitored and publically reported.[23 24] Reports showed that the post-operative VTE incidence rates have nearly halved in U.S. hospitals in recent years,[24 25] and post-VTE mortality rate declined by a third within a decade since the mid-90s.[26] These rate decreases may be, in part, due to the implementation of post-operative VTE prevention protocols,[27] however substantial variation in post-operative VTE incidence rate was also evident among U.S. hospitals.[25] Although patients case mix and surgery types may play a role in such differences,[6 28 29] the variation of VTE incidence among the same type of hospitals over time and within the group may reflect the success of quality improvement interventions and demonstrate the potential for further development.[30 31]

Few Australian studies have reported VTE incidence,[3 8 32] and the measures of VTE used in these studies varied making comparison difficult. Consequently, we employed the internationally-recognised AHRQ measures for post-operative VTE, and subsequent mortality, to explore the trend of the incidence rates and their variations among admitted surgical patients in acute public hospitals across New South Wales (NSW), Australia (2002-2009).

METHODS

Data source and study population

New South Wales is the largest health jurisdiction in Australia with approximately 497 healthcare facilities and a population of over seven million people. We used records from the NSW Admitted

Patient Data Collection (APDC) database, which includes all admitted patient services provided by NSW public and private healthcare facilities. The APDC includes information on patient demographics, medical conditions and procedures, hospital characteristics, and separations (discharges, transfers and deaths) from all public and private hospitals (as well as day procedure centres) in NSW. The medical records for each episode of care in the APDC were assigned with codes based on the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification (ICD-10-AM) 4th edition.[33] Of admissions at 497 healthcare facilities across NSW between 1st January 2002 to 31st December 2009, we included all 82 NSW acute public hospitals (9,221,128 admissions; 57.4%) in our study. Two children's hospitals and one other hospital (data was unavailable) were excluded We restricted our study to only elective surgical patients and applied the same AHRQ inclusion criteria[23] for patients who had elective surgery within two days of admission, aged between 18 – 90 years (inclusive), and were not transferred to another acute care facility (4,362,624 episodes (47.3%)). Ethical approval was obtained from the University of NSW Human Research Ethics Committee (LNR/11/CIPHS/64).

Measures and covariates

Of surgical ~~P~~patients who met AHRQ inclusion criteria (patients at risk), those who developed VTE were identified by secondary diagnostic codes (ICD-10-AM) translated from the AHRQ definition (ICD-9-CM) by Victorian Government Health Information.[34] The outcome measure was teremed "post-operative VTE", proposed by the Australian version of patient safety indicators (AusPSI),[35] instead of "peri-operative VTE" term suggested by AHRQ.[23] We used "post-operative VTE" since employment of inclusing criteria (undergoing surgery within two days of admission and secondary diagnosis of VTE) miminmised likelihood of VTE presence on admission or VTE occurance prior surgery.~~We employed the term "post-operative VTE" from the Australian version of patient safety indicators (AusPSI)[35] instead of "peri-operative VTE" developed by AHRQ.~~ In combination with discharge status, patients post-VTE outcomes were categorised as survival or death. VTE and related death rates were presented as incidences per 1000 admissions within each year between 2002 and 2009, inclusively.

Two sets of patient- and hospital-related covariates were considered. Patient demographic variables included age, gender, country of birth, marital status, patient socio-economic status, and principle diagnostic disease groups (the ten most common) within the study population. We utilised a postcode-level advantage and disadvantage index of Socio-Economic Indices for Areas (SEIFA) with the lower values indicating more disadvantaged areas.[36] SEIFA scores were categorised into four classes (1st quartile = most disadvantaged areas and 4th quartile = most advantaged areas). The disease groups

were identified using principle diagnostic codes (ICD-10-AM) at admissions through the methodology develop by Quan et al..[37] Using relevant procedure codes from ICD-10-AM (Appendix 1), we defined six major surgical procedures including coronary-artery bypass graft (CABG), abdominal aortic aneurysm (AAA) repair, total hip replacement, total knee replacement, cholecystectomy, and other surgical procedures.

Hospital covariates included the local health district (metropolitan, rural and regional NSW) and peer group (A1: principal referral group, usually teaching hospitals; A3: ungrouped acute; B: major metropolitan and non-metropolitan; C1: district group 1; and, C2: district group 2). Hospital peer groups contained similar type and sized hospitals, ranging from those treating more than 25,000 acute case-mix weighted separations per annum in principal referral groups through to treating 2,000^{+} (but less than 5,000) acute case-mix weighted separations per annum in district group 2.[38]

Statistical analysis

We employed Poisson mixed models to evaluate adjusted incidence rates and rate ratios for study outcomes after including all patients and hospital-related characteristics. A random intercept term was utilised to incorporate any clustering effect at hospital-level. To investigate the temporal behaviour of the outcomes, calendar years were entered into the model as indicator variables, with 2002 as the reference year. A model with the year as a continuous variable was also examined for linear trends. We derived hospital peer group and surgery type trends using interaction effects (year and hospital peer group; year and surgery type) in separate models. Adjusted incidence rates for specific years were derived by multiplying yearly-adjusted risk ratios to the crude risks observed in the reference year.

We initially examined the Elixhauser and the Charlson Index comorbidities based on the ICD-10 coding scheme,[37] however we did not include either of them in the models given an unexpected drop in the comorbidity index among our study population in recent years (Appendix 2) and also recent reports that these indices may introduce misleading results possibly due to geographical variations and biases in the coding.[39-41] To study the variation of outcomes across hospitals within each hospital group, hospital-specific random intercept components were extracted from Poisson mixed models constructed for each hospital group, then ranked and categorised into five classes at 20% incremental quintiles. To obtain adjusted differences between those with the highest and those with the lowest VTE incidence, the adjusted classes were entered into a Poisson model including patient characteristics covariates. We used Pearson correlation to assess the association of hospital performances between VTE and post-VTE deaths, based on the hospital-specific random intercepts. All analyses were performed in R package version 3.0.0[42] and Stata^{TM} 11.0.[43]

RESULT

~~Table 1~~ Table 1 summarised the study population by outcomes across hospital and patient characteristics and related statistics. Of the 4,223,317 (45.8% of all admissions with no missing information) elective surgical admissions during 2002-2009 with a median length of stay of one day (the first (Q1) and the third quartiles (Q3) equal to one day), 8,451 patients developed either DVT or PE after surgery, resulting in an incidence rate of 2 per 1000 surgical patients with a median length of stay of 11 days (Q1=6 and Q3=21days). Among them, 673 (8%) died prior to discharge ~~(8%)~~with a median length of stay of 11 days (Q1=4 and Q3=22 days); 79.6 per 1000 patients with post-operative VTE. Compared to females, males tended to have a lower risk of post-operative VTE (IRR=0.91); however, they were more likely to die (IRR=1.19) following a VTE. Older patients were exposed to higher risks of VTE and death after surgery. Married patients and those who were born in Europe (except the UK), Asia and North Africa experienced a lower risk of post-operative VTE compared to their counterparts but a similar risk of post-VTE death.

Patients admitted with malignancy and congestive heart failure had the highest VTE and hospital mortality rates. Patients who underwent total knee replacement, AAA repair and total hip replacement surgeries had higher risk of VTE, respectively; however, post-VTE mortality was lower among orthopaedic surgical patients compared to other procedures. Higher socio-economic status (quartiles of SEIFA) of patients was associated with a lower risk of VTE. There was no difference in mortality for patients residing in advantaged and disadvantaged areas. Patients from principal referral hospitals were more likely to acquire VTE in comparison to the patients from district hospitals (IRR= 0.56 and 0.37 for group 1 and 2 hospitals respectively). No differences in outcomes were observed between metropolitan and non-metropolitan hospitals.

Post-operative VTE incidence rate significantly increased over the study period by 30%, from 1.77 per 1000 patients in 2002 to 2.30 in 2009 (Figure 1). Despite some fluctuation, all hospital peer groups exhibited similar increasing trends in post-operative VTE incidence over the study period after adjustment for patient demographics (Figure 2), ranging from 19% (2.58 vs. 2.17) in principal referral hospitals to 237% (1.21 vs. 0.36) in district group 2. Surgery-specific VTE rates for the five procedures exhibited high fluctuations and insignificant trends, whereas the other surgery group showed a steady increasing trend of 38% (3.01 vs. 2.18) over the study period (Figure 3). Post-VTE mortality fluctuated between 68 to 97 cases per 1000 patients over the study period with no significant change after adjusting for confounders overall (Figure 1) and at hospital peer group level (Figure 2). Mortality tended to be stable across hospital peer groups as between-group variation of mortality

reduced over the study period. No surgery-specific trend analysis was conducted due to small number of post-DVT deaths per annum.

The incidence rate ratios between those hospitals with the lowest, and those with the highest rate, was larger in VTE related mortality than in VTE and varied across hospital peer group (~~Table 2~~Table 2). For VTE, the difference in rate is less than four-fold in the principal referral and major peer groups (include large hospitals) but at least eight-fold in district peer groups (include small hospitals). Similarly, the difference in rate is larger in district group 1 and 2 (IRR=23 and 38) compared to principal referral (IRR=1.7) and major metropolitan/non-metropolitan hospitals (IRR=15) for VTE related deaths. The close to significant negative correlation (-0.45, P-value=0.057) for principal referral hospitals implied that hospitals with the highest post-operative VTE rate tended to have a lower rate of subsequent death. In contrast, within district group 2 (0.41), hospitals with higher VTE rates tended to also have the highest post-VTE death rates. There were no such associations within other peer groups.

Table 1. Study population, incidence rates (IR) and adjusted incidence rate ratios (IRR) of surgical patients who developed VTE and died, stratified by patient and hospital characteristics.

Characteristics	Surgical patients n (%)	VTE			VTE associated death		
		Frequency (%)	IR	IRR (95% CI)	Frequency (%)	IR	IRR (95% CI)
Sex							
Female	2280384 (54.00)	4626 (54.74)	2.03	1.00	330 (49.03)	71.34	1.00
Male	1942933 (46.00)	3825 (45.26)	1.97	0.90 (0.86-0.94) **	343 (50.97)	89.67	1.19 (1.02-1.40) *
Age							
>=18yr & <35yr	738382 (17.48)	487 (5.76)	0.66	0.21 (0.19-0.23) **	11 (1.63)	22.59	0.20 (0.11-0.37) **
>=35yr & <55yr	1013921 (24.01)	1308 (15.48)	1.29	0.42 (0.40-0.45) **	82 (12.18)	62.69	0.58 (0.45-0.74) **
>=55yr & <75yr	1595024 (37.77)	3538 (41.86)	2.22	0.66 (0.63-0.70) **	290 (43.09)	81.97	0.85 (0.72-1.01)
>=75yr & <90	875990 (20.74)	3118 (36.90)	3.56	1.00	290 (43.09)	93.01	1.00
Marital status							
Married	2548508 (60.34)	4667 (55.22)	1.83	1.00	381 (56.61)	81.64	1.00
Single	1674809 (39.66)	3784 (44.78)	2.26	1.16 (1.11-1.21) **	292 (43.39)	77.17	1.01 (0.86-1.18)
Country of birth							
Australia and New Zealand	2839135 (67.23)	5858 (69.32)	2.06	1.00	479 (71.17)	81.77	1.00
UK, US & Canada	239088 (5.66)	645 (7.63)	2.70	1.06 (0.97-1.15)	53 (7.88)	82.17	0.95 (0.72-1.27)
Non-English Europe	447239 (10.59)	1046 (12.38)	2.34	0.74 (0.69-0.80) **	80 (11.89)	76.48	0.91 (0.71-1.16)
North Africa	130938 (3.10)	139 (1.64)	1.06	0.47 (0.40-0.56) **	9 (1.34)	64.75	0.87 (0.45-1.70)
Asia	179725 (4.26)	193 (2.28)	1.07	0.45 (0.39-0.52) **	16 (2.38)	82.90	1.09 (0.66-1.80)
Others	387192 (9.17)	570 (6.74)	1.47	0.58 (0.53-0.64) **	36 (5.35)	63.16	0.95 (0.67-1.35)
Major surgical procedure							
AAA repair	1744 (0.04)	26 (0.31)	14.91	1.00	6 (0.89)	230.77	1.00
CABG	10529 (0.25)	52 (0.62)	4.94	0.37 (0.23-0.60) **	7 (1.04)	134.62	0.69 (0.23-2.10)
Cholecystectomy	50145 (1.19)	42 (0.50)	0.84	0.09 (0.05-0.15) **	6 (0.89)	142.86	0.70 (0.22-2.22)
Total hip replacement	18771 (0.44)	207 (2.45)	11.03	0.74 (0.49-1.11)	4 (0.59)	19.32	0.12 (0.03-0.44) **
Total knee replacement	29428 (0.70)	798 (9.44)	27.12	1.76 (1.19-2.61) **	3 (0.45)	3.76	0.03 (0.01-0.11) **
Other	4112700 (97.38)	7326 (86.69)	1.78	0.17 (0.11-0.24) **	647 (96.14)	88.32	0.52 (0.23-1.19)
Major principle diagnostic diseases†							
Cardiac arrhythmias	25953 (0.61)	75 (0.89)	2.89	-	2 (0.30)	26.67	-
Chronic pulmonary disease	11558 (0.27)	69 (0.82)	5.97	-	6 (0.89)	86.96	-
Coagulopathy	3908 (0.09)	37 (0.44)	9.47	-	2 (0.30)	54.05	-
Congestive heart failure	6765 (0.16)	85 (1.01)	12.56	-	17 (2.53)	200.00	-
Diabetes with chronic complication	33541 (0.79)	79 (0.93)	2.36	-	11 (1.63)	139.24	-

Malignancy including lymphoma & leukaemia	150962 (3.57)	1070 (12.66)	7.09	-		182 (27.04)	170.09	-
Metastatic solid tumour	19699 (0.47)	291 (3.44)	14.77	-		67 (9.96)	230.24	-
Peripheral vascular disease	15993 (0.38)	141 (1.67)	8.82	-		10 (1.49)	70.92	-
Renal failure	1385753 (32.81)	42 (0.50)	0.03	-		1 (0.15)	23.81	-
Rheumatoid arthritis/collagen vascular disease	10748 (0.25)	40 (0.47)	3.72	-		1 (0.15)	25.00	-
Year								
2002	431184 (10.21)	763 (9.03)	1.77	1.00		65 (9.66)	85.19	1.00
2003	438058 (10.37)	780 (9.23)	1.78	1.01 (0.92-1.12)		53 (7.88)	67.95	0.85 (0.59-1.22)
2004	462451 (10.95)	878 (10.39)	1.90	1.09 (0.99-1.20)		65 (9.66)	74.03	0.82 (0.58-1.16)
2005	508097 (12.03)	1038 (12.28)	2.04	1.17 (1.07-1.29)	**	75 (11.14)	72.25	0.77 (0.55-1.08)
2006	550688 (13.04)	1062 (12.57)	1.93	1.11 (1.01-1.22)	*	103 (15.30)	96.99	1.02 (0.74-1.40)
2007	591973 (14.02)	1223 (14.47)	2.07	1.22 (1.12-1.34)	**	87 (12.93)	71.14	0.72 (0.52-1.01)
2008	607631 (14.39)	1313 (15.54)	2.16	1.27 (1.16-1.38)	**	112 (16.64)	85.30	0.90 (0.66-1.23)
2009	633235 (14.99)	1394 (16.50)	2.20	1.30 (1.19-1.42)	**	113 (16.79)	81.06	0.83 (0.60-1.13)
Year-linear trend	-	-	-	1.04 (1.03-1.05)	**	-	-	0.98 (0.95-1.02)
Quartiles of SEIFA								
1st quartile (most disadvantaged)	1089833 (25.81)	2308 (27.31)	2.12	1.00		187 (27.79)	81.02	1.00
2nd quartile	1084727 (25.68)	1981 (23.44)	1.83	0.88 (0.82-0.94)	**	169 (25.11)	85.31	0.96 (0.78-1.20)
3rd quartile	1074283 (25.44)	2088 (24.71)	1.94	0.76 (0.72-0.81)	**	175 (26.00)	83.81	1.04 (0.84-1.30)
4th quartile (most advantaged)	974474 (23.07)	2074 (24.54)	2.13	0.70 (0.65-0.75)	**	142 (21.10)	68.47	0.98 (0.77-1.26)
Peer hospital groups								
Principal referral	2269392 (53.73)	5141 (60.83)	2.27	1.00		381 (56.61)	74.11	1.00
Ungrouped acute	133465 (3.16)	380 (4.50)	2.85	1.20 (0.54-2.66)		43 (6.39)	113.16	0.94 (0.37-2.39)
Major metro- & non-metropolitan	1140036 (26.99)	2125 (25.14)	1.86	0.84 (0.54-1.31)		183 (27.19)	86.12	0.96 (0.60-1.55)
District group 1	346910 (8.21)	484 (5.73)	1.40	0.56 (0.33-0.95)	*	42 (6.24)	86.78	0.99 (0.54-1.83)
District group 2	333514 (7.90)	321 (3.80)	0.96	0.37 (0.23-0.61)	**	24 (3.57)	74.77	0.74 (0.38-1.44)
Local health district								
Metropolitan	2720690 (64.42)	5882 (69.60)	2.16	1.00		430 (63.89)	73.10	1.00
Rural & Regional NSW	1502627 (35.58)	2569 (30.40)	1.71	0.74 (0.52-1.05)		243 (36.11)	94.59	1.26 (0.82-1.92)
Total	4223317	8451	2.00	-		673	79.64	-

139,307 (3.2%) cases were excluded due to missing or unknown items.
Incidence rates (IR) are crude and reported per 1000 patients.
Risk ratios (RR) and related confident intervals (CI) were obtained using a Poisson mixed model.
CABG: Coronary Artery Bypass Graft; AAA repair: Abdominal Aortic Aneurysm repair.
† No RR is reported since this characteristic has not been included in the Poisson mixed model.
* Significant at 5%; ** significant at 1%.

Table 2. Incidence rates (IR), adjusted incidence rate ratios (IRR) and association of outcomes between the best and worst performers (top and bottom 20% quintiles) within hospital peer groups

Hospital peer group	Hospital n	VTE				Post-VTE death				Correlation coefficient (95% CI)
		Lowest (IR)	Highest (IR)	IRR (95% CI)		Lowest (IR)	Highest (IR)	IRR (95% CI)		
Principal referral	17	1.24	4.00	3.70 (3.32-4.12)	**	43.58	131.12	1.78 (1.30-2.44)	**	-0.45 (-0.79, 0.01)
Major metro- & non-metropolitan	22	1.00	2.99	3.85 (3.33-4.46)	**	16.80	162.30	15.48 (6.45-37.12)	**	0.15 (-0.28,0.54)
District group 1	13	0.42	3.71	8.64 (6.23-11.98)	**	13.88	242.71	38.02 (10.25-140.94)	**	-0.37 (-0.76,0.22)
District group 2	30	0.22	2.15	8.92 (5.49-14.49)	**	16.66	104.97	23.26 (2.94-183.50)	**	0.41 (0.05,0.68) *

Incidence rates (IR) are crude and reported per 1000 patients.
Risk ratios (RR) and related confident intervals (CI) were obtained using a Poisson model and adjusted for patient characteristics. Those hospitals with the lowest rate were set as the reference level.
Ungrouped acute group was removed from analysis due to small number of hospitals within this group.
* Significant at 5%; ** significant at 1%.

DISCUSSION

In this large cohort study, of elective surgical patients, from all NSW acute public hospitals, over an 8 year period, we found that the incidence of VTE to be two of 1000 elective surgical admissions, and VTE associated mortality to be 8%. The adjusted incidence of VTE increased significantly over the study period (30%), with no change in mortality. There were significant differences in incidence of VTE between hospital peer groups and between hospitals with the lowest and those with the highest rate. Principal referral hospitals exhibited a higher overall incidence, but lower intragroup variation compared to other peer groups. Principal referral hospitals with a higher incidence of VTE also tended to have a lower VTE-related mortality.

The incidence of post-operative VTE in NSW hospitals was less than half that of. U.S. hospitals within a similar period (4.5 or more per 1000 patients in 2010 and prior),[25 44] but with a similar VTE associated mortality (83 vs. 79 per 1000 patients). [25] Based upon our findings, VTE incidence and associated mortality contributes to approximately 15% and 8% of overall failure-to-rescue (FTR)-related incidence and mortality (13.8 and 140 per 1000 patients, respectively).[45 46] Despite the fact that our study and the U.S. study used the identical measure defined by AHRQ,[23] the discrepancies and coding practices between the U.S. (ICD-9-CM) and Australia (ICD-10-AM) may, in part, have contributed to the difference. It was shown that accuracy of VTE coding can be improved by the adoption of extended codes developed in the revised ICD-9-CM. [47]

In a recent Organization for Economic and Co-Operation and Development (OECD) report, Australian-wide incidence were 0.97 and 1.26 per 1000 patients in 2009 and 2012 respectively, placing Australia among three nations (Australia, Slovenia and the U.S.) with the highest incidence of approximately one per a thousand surgical patients or more within the last decade.[48] Our observed rate for NSW hospitals was nearly double that of the OCED provided Australian rates, possibly due to the fact that we studied only elective surgical patients from acute public hospitals. Such cross-nations reports provide a platform for health service comparisons and the study of longitudinal variations. However, internal and external comparability of OCED results may be affected by the heterogeneity and biases of the different nation's coding systems.

Despite continued poor compliance with VTE prevention guidelines and VTE preventative measures,[49-52] post-operative VTE incidence in U.S. hospitals almost halved between 2007-2011.[24 44] In Australia, given the overt gap between evidence and practice of VTE prevention protocols,[53 54] the National Institute of Clinical Studies (NICS) launched a VTE prevention program in 85 public and private hospitals across Australia between 2005-2008 which resulted in

increased awareness of and adherence with VTE prevention guidelines.[2 55] However, we found an increasing trend in NSW post-operative VTE incidence rate within 2002-2009, with an approximate 4% annual increase and total increase of 30%, mostly contributed by the higher incidence in the smaller hospital peer groups (237%) compared to the large teaching hospital group (19%). The reason for this increase is unclear.

Our finding of a higher incidence of VTE and VTE associated mortality with increasing age is similar that observed by others.[29 56-58] Ageing previously accepted as a major contributing factor to the increasing trends in VTE rates for admitted patients in Australian hospitals.[3] However, we have taken into account patient characteristics including age as well as surgery type and demonstrated an adjusted increasing trend for surgical patients, despite the observed decreasing trends in proportions of AAA repair and orthopaedic surgical procedures (Appendix 2) known with high post-operative VTE risks (Table 1).[1] Notably, the steadily increasing VTE incidences among patients who underwent other surgical procedures mainly contributed to the observed overall trend (Figure 3). More research is required to examine the contributing factors for such a difference among different surgical procedures. In particular, comorbidity-specific analysis at hospital level is encouraged to minimise potential biases reported elsewhere.[39-41]

Although other studies suggest gender may not be a significant risk factor for VTE,[28 29 59] we found males were less likely to develop VTE complications, but more likely to subsequently die. We did not separately explore DVT and PE incidence and associated deaths between genders; but our higher mortality risk for males can be explained by the estimated higher odds of PE (vs. DVT which has a lower risk of death[29 59] for males compared to females (1.87 vs. 1.02 respectively) in Australian hospitals during our study period.[3]

Variation in the application of VTE prevention guidelines and other quality initiatives may have contributed to the differences in outcomes amongst the hospitals in our study. Smaller, district 1 and 2 peer groups hospitals, had a significantly lower VTE incidence rate compared to larger hospitals in NSW. This was in contrast with other studies which showed that larger hospitals have a lower mortality following major procedures, such as orthopaedic surgeries[60 61] and post-operative complications such as VTE.[62] A possible explanation for this discrepancy is that principal referral hospitals undertook higher risk patients and surgical complexity than the smaller district hospitals. Geographical variations in coding,[39-41] underreporting of VTE due to mis-coding to a more general cardiovascular item,[3 63] and high diagnosis likelihood of high-risk but asymptomatic post-operative patients[64] may also have contributed to elevated VTE rates in major hospitals. We did not observe differences between NSW hospital peer groups for VTE mortality, nor did other studies for

FTR rates. However, we did observe greater variation in VTE mortality within peer groups comprising smaller sized hospitals in comparison to larger principal referral hospitals.

Our study showed a significant performance difference between hospitals, within each hospital peer group, with the highest and those with the lowest VTE incidence and associated mortality. Similarly, the association between the two outcomes also varied across groups. Smaller hospitals (district groups 1 and 2) exhibited larger differences in both outcomes, suggesting a greater variability of patient care practice and outcomes amongst this group of hospitals and the greater potential for intervention aimed at VTE prevention and treatment for this group. We also noted a positive association between VTE incidence and VTE mortality amongst smaller size hospital groups. In contrast, larger NSW hospitals tended to have a higher VTE incidence but lower VTE associated mortality, suggests that there may be a volume-outcome relationship or a greater adherence to evidence-based prevention and treatment guidelines that may explain this better VTE associated mortality. Interestingly, if the higher incidence of VTE alone was used as a measure of failure-to-prevent, these hospitals may be considered to have performed poorly overall, despite the better VTE associated mortality. Conversely, if the higher incidence rates of VTE were largely due to patient selection and case-mix, these hospitals could be considered as better quality hospitals having a lower failure-to-rescue rate with better treatment outcomes. Further investigation into the factors that may explain these differences and the ideal reporting measures is warranted.

Our study raised several important policy implications. Firstly, despite the fact that national and state agencies had developed evidence-based guidelines, such as the Clinical Excellence Commission of NSW "Medication Safety",[65] in which VTE prevention practices were promoted and related incidents evaluated, the increasing incidence of VTE and unchanged VTE mortality question the effectiveness of current national policy and local programs in reducing VTE incidence and mortality. Secondly, the development of systematic local program based on relevant international experience in successfully reducing VTE rate and its related mortality needs urgent policy action. Thirdly, the large variability of VTE rate and its related mortality between and within different hospital peer groups suggests that there is room for improvement in both the prevention and treatment of VTE and that VTE still remains a preventable complication. Lastly, as an important indicator of the quality of care, the level of standardised reporting of VTE in Australia should be explored.

The strengths of our study are that it is the first population-based observational study across all acute public hospitals within the one (i.e. NSW) health region. We used a standardised measure and presented both incidence rates of VTE and VTE associated mortality, thus enabling to differentiate between the two outcome measures and allow for international comparisons. Limitations of our study

include that we specifically studied only elective surgical patients according to AHRQ definitions; whereas the analyses of all patient populations may provide addition insight. Future research needs to provide more evidence on the whole inpatient population. We also may have under-reported our findings because of possible coding discrepancies. Nevertheless, this study reinforced the importance of developing measures for combating post-operative VTE, and the continual monitoring and public reporting VTE incidence and mortality.[2 66]

CONCLUSION

The significant increase in VTE incidence among surgical patients over an eight-year period, and persisting level of VTE associated mortality, highlights the need for urgent policy interventions. The significant variation for both outcomes between, and within, different hospital peer groups suggests room for improvement in both the prevention and treatment of VTE. Routine measurement and disclosure of both VTE incidence and associated mortality can provide policy-makers, clinicians and researchers with opportunities to monitor and adjust for performance.

CONTRIBUTORS

Conceived and designed the study: HA, JC, AF, and KH. Prepared the data and performed the analyses: HA, JC, and LO. Wrote the paper: HA, JC, SH, AF, and KH.

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COMPETING INTERESTS

Authors had no conflict of interest.

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No additional data are available.

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APPENDIX

1. Procedure codes from ICD-10-AM for selected surgical procedures

Procedure category	Code			
Abdominal aortic aneurysm	33112-00	33151-00		
	33115-00	33157-00		
	33118-00	33154-00		
	33121-00	33160-00		
Coronary artery bypass graft	38497-00	38500-00	38503-01	90201-00
	38497-01	38500-01	38503-02	90201-01
	38497-02	38500-02	38503-03	90201-02
	38497-03	38500-03	38503-04	90201-03
	38497-04	38500-04		
	38497-05	38503-00		
	38497-06			
	38497-07			
Cholecystectomy	30443-00	30454-01		
	30445-00	30455-00		
	30446-00			
	30448-00			
	30449-00			
Total hip replacement	49318-00	49330-00		
	49319-00	49333-00		
	49324-00	49345-00		
	49327-00			
Total knee replacement	49518-00	49527-00		
	49519-00	49534-00		
	49521-00	49530-00		
	49521-01	49530-01		
	49521-02	49533-00		
	49521-03	49554-00		
	49524-00			
	49524-01			

2. Patient mix over the study period.

Characteristic	Year								Total
	2002	2003	2004	2005	2006	2007	2008	2009	
Age (mean, IQ)	55.77 (40-72)	55.87 (40-72)	56.05 (40-72)	56.40 (40-73)	57.23 (41-74)	57.70 (42-74)	57.97 (43-74)	58.54 (44-74)	55.77 (41-73)
Charlson index (mean, IQ)	0.66 (0-2)	0.69 (0-2)	0.72 (0-2)	0.73 (0-2)	0.71 (0-2)	0.70 (0-2)	0.49 (0-0)	0.32 (0-0)	0.61 (0-1)
Surgery (n, %)									
AAA repair	269 (0.06)	272 (0.06)	252 (0.05)	241 (0.05)	208 (0.04)	199 (0.03)	173 (0.03)	130 (0.02)	1744 (0.04)
CABG	1523 (0.35)	1588 (0.36)	1369 (0.30)	1220 (0.24)	1299 (0.24)	1220 (0.21)	1228 (0.20)	1082 (0.17)	10529 (0.25)
Cholecystectomy	6083 (1.41)	6235 (1.42)	5971 (1.29)	6202 (1.22)	6687 (1.21)	6426 (1.09)	6560 (1.08)	5981 (0.94)	50145 (1.19)
Hip replacement	2079 (0.48)	2113 (0.48)	2129 (0.46)	2415 (0.48)	2415 (0.44)	2375 (0.40)	2623 (0.43)	2622 (0.41)	18771 (0.44)
Knee replacement	3019 (0.70)	2954 (0.67)	3043 (0.66)	3970 (0.78)	4297 (0.78)	4026 (0.68)	4106 (0.68)	4013 (0.63)	29428 (0.70)
Other	418211 (96.99)	424896 (97.00)	449687 (97.24)	494049 (97.24)	535782 (97.29)	577727 (97.59)	592941 (97.58)	619407 (97.82)	4112700 (97.38)

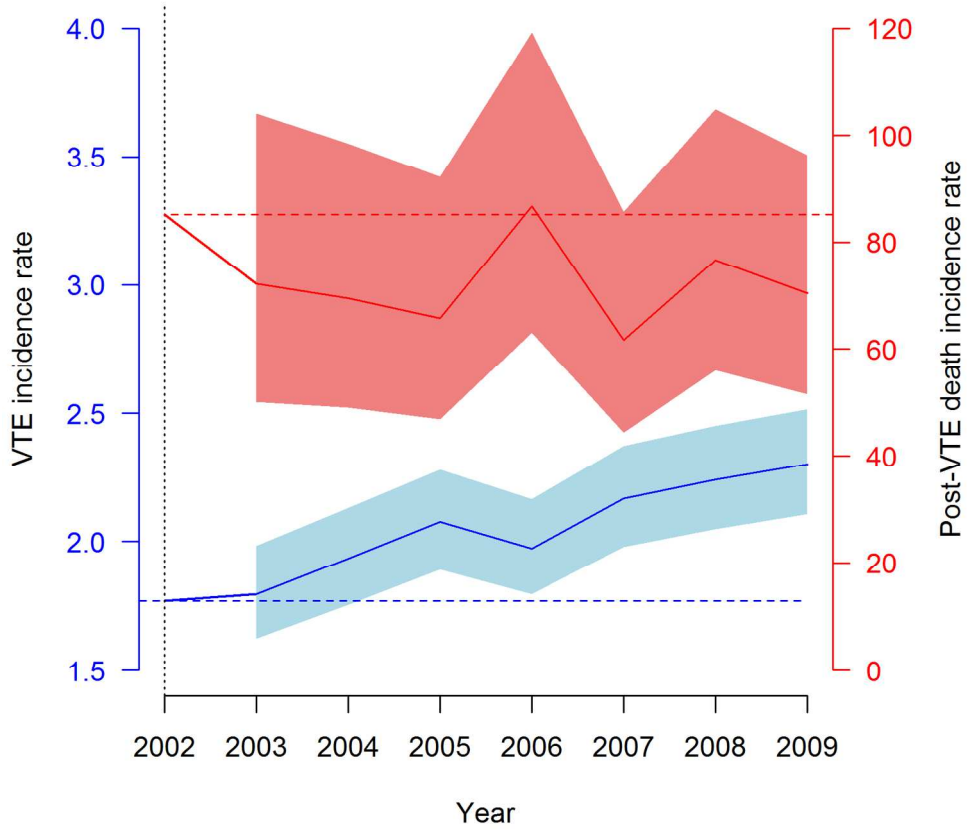
IQ: Interquartile; CABG: Coronary Artery Bypass Graft; AAA repair: Abdominal Aortic Aneurysm repair.

FIGURE LEGENDS

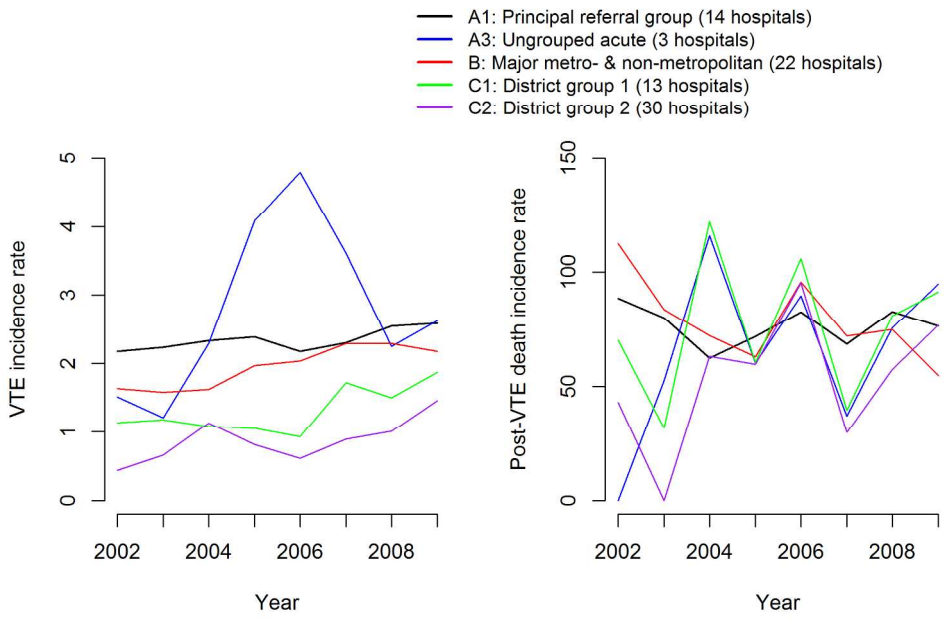
Figure 1. Adjusted trends of post-operative VTE and post-VTE death incidence rates (per 1000 elective surgical patients, and 1000 patients with post-operative VTE respectively) over the study period. Rates were estimated by multiplying incidence rate ratio (obtained from the Poisson mix model) and crude risk at the reference year (2002).

Figure 2. Hospital peer group-specific adjusted trends of post-operative VTE (left panel) and post-VTE death (right panel) incidence rates (per 1000 elective surgical patients, and 1000 patients with post-operative VTE respectively) over the study period. Rates were estimated by multiplying incidence rate ratio (obtained from the Poisson mix model including an interaction term for "hospital peer group × year") and crude risk of the reference hospital group (Principal referral) at the reference year (2002).

Figure 3. Surgical procedure-specific adjusted trends of post-operative VTE incidence rates (per 1000 elective surgical patients) over the study period. Rates were estimated by multiplying incidence rate ratio (obtained from the Poisson mix model including an interaction term for "surgery type × year") and crude risk of the reference surgery group (AAA repair) at the reference year (2002).



152x152mm (300 x 300 DPI)



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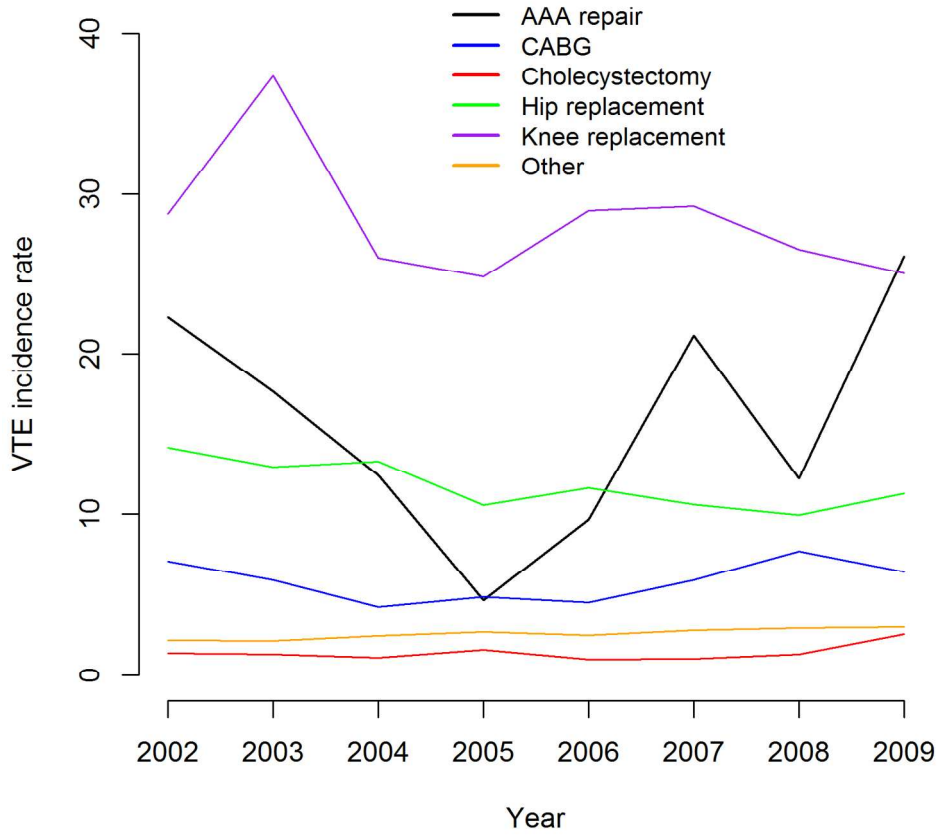

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STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any pre-specified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5-6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	5
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-6
Bias	9	Describe any efforts to address potential sources of bias	6
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5-6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	6
		(*c*) Explain how missing data were addressed	6 , 8-Table 1
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	NA

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	6 (partly)
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8-Table 1
		(b) Indicate number of participants with missing data for each variable of interest	NA
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	NA
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	NA
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	NA
		Cross-sectional study—Report numbers of outcome events or summary measures	8-Table 1
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6-10(Tables 1 & T)
		(*b*) Report category boundaries when continuous variables were categorized	5, 8-10(Tables 1 & T)
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7, Figure 2
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11, 12 , 14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11-14
Generalisability	21	Discuss the generalisability (external validity) of the study results	11, 12, 14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.