Variation in the risk of venous thromboembolism following colectomy

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Background: Guidelines recommend extended thromboprophylaxis following colectomy for malignant disease, but not for non-malignant disease. The aim of this study was to determine absolute and relative rates of venous thromboembolism (VTE) following colectomy by indication, admission type and time after surgery.

Methods: A cohort study of patients undergoing colectomy in England was undertaken using linked primary (Clinical Practice Research Datalink) and secondary (Hospital Episode Statistics) care data (2001–2011). Crude rates and adjusted hazard ratios (HRs) were calculated for the risk of first VTE following colectomy using Cox regression analysis.

Results: Some 12 388 patients were identified; 312 (2.5 per cent) developed VTE after surgery, giving a rate of 29.59 (95 per cent c.i. 26.48 to 33.06) per 1000 person-years in the first year after surgery. Overall rates were 2.2-fold higher (adjusted HR 2.23, 95 per cent c.i. 1.76 to 2.50) for emergency compared with elective admissions (39.44 *versus* 25.78 per 1000 person-years respectively). Rates of VTE were 2.8-fold higher in patients with malignant disease *versus* those with non-malignant disease (adjusted HR 2.84, 2.04 to 3.94). The rate of VTE was highest in the first month after emergency surgery, and declined from 121.68 per 1000 person-years in the first month to 25.65 per 1000 person-years during the rest of the follow-up interval. Crude rates of VTE were similar for malignant and non-malignant disease (114.76 *versus* 120.98 per 1000 person-years respectively) during the first month after emergency surgery.

Conclusion: Patients undergoing emergency colectomy for non-malignant disease have a similar risk of VTE as patients with malignant disease in the first month after surgery.

+A: Introduction

More than 33 000 colectomies are performed in England each year, and nearly 250 000 in the USA, for non-malignant and malignant disease, with nearly one-quarter occurring as an emergency procedure[1]. Recent international guidance has recommended that patients undergoing colectomy for malignant disease should receive extended pharmacological thromboprophylaxis for 4 weeks after surgery, based on evidence from four randomized trials

including 901 patients, of whom over 80 per cent had malignant disease[2–5]. A subsequent systematic review[6] of these studies reported a reduction in overall venous thromboembolism (VTE) from 14.3 to 6.1 per cent (odds ratio 0.41, 95 per cent c.i. 0.26 to 0.63). However, no such evidence exists for patients undergoing colectomy for non-malignant disease, who account for 40–50 per cent of patients having a colectomy[7,8]. Hence, no specific guidance has been issued on extended VTE prophylaxis in this group, despite these patients having underlying medical conditions such as ulcerative colitis, Crohn's disease and diverticular disease that are associated with an inherent increased risk of VTE compared with that in the general population, in both the ambulatory and hospital setting[9–11]. Previous studies describing the risk of VTE following colectomy for non-malignant disease have had limited follow-up (30 days), reducing their ability to quantify the highest risk period for VTE following surgery[7,12]. Similarly, studies reporting the risk of VTE following colectomy for malignant disease have used a limited 30-day follow-up[13], or have compared the risk of VTE after colectomy with that in patients with advanced metastatic disease, and hence have concluded, probably erroneously, that the risk of VTE is reduced after surgery[14].

Published studies on VTE following colectomy have failed to quantify the risk in terms of indication for surgery (particularly non-malignant indications), timing of surgery (emergency *versus* elective), and duration or timing of the highest risk of VTE after operation. The aim of the present study was to determine the magnitude and duration of risk of VTE following colectomy by indication for surgery and timing of surgery using linked electronic healthcare data from England[15].

+A: Methods

The study was approved by the Independent Scientific Advisory Committee approval board (Protocol 11-051R).

+B: Data sources

The Clinical Practice Research Database (CPRD) is a primary care database containing diagnostic and prescription data for approximately 13 million people of the general population in the UK, with 3·4 million active patients contributing data. Diseases are coded within the CPRD using Read codes which have been used by clinicians to record data within primary care since 1985.[16]

Hospital Episode Statistics (HES) collects a record for each episode of admitted patient care delivered in England, either by National Health Service (NHS) hospitals or delivered in the independent sector but commissioned by the NHS. It has collected data since 1989, with more than 15 million new records added each year. Records are coded using a combination of ICD-10 codes for diagnosis at discharge along with Office of Population, Censuses and Surveys Classification of Surgical Operations and Procedures (OPCS 4) detailing procedures performed. Increasingly HES data are being used to study surgical diseases, with a recent systematic review[17] reporting that approximately two-thirds of studies published using these data concern surgical conditions.

Death certificate data from the Office for National Statistics were also used. Anonymized patient identifiers from CPRD and HES were linked by a trusted third party by using the NHS number, date of birth, postcode and sex. Most patients were matched exactly according to NHS number (over 90 per cent of patients are linked in this way), with the remaining patients linked probabilistically on the basis of postcode, date of birth and sex. In the version employed, 53.0 per cent of practices in the CPRD are linked to HES, representing a 3.0 per cent sample of the population of England. These data have been shown previously[18] to be similar in terms of age, sex and geographical distribution to data from the UK population.

+B: Cohort

The cohort was identified using OPCS codes for any colectomy from HES data between 2001 and 2011 (*Appendix S1*, supporting information). Operations confined to or including the rectum and anal canal were excluded. Person-time at risk commenced on the day after surgery for the overall analysis; therefore VTEs recorded on the same day as the operation were not included in the analysis. Patients were followed up until they developed a VTE event, died, left a participating general practice, or for 1 year after surgery. Patients were excluded if they were: not in a linked general practice or had had a VTE before the admission date for colectomy, as these patients have an inherently increased risk of postoperative VTE. Previous VTE was defined using the same definition as for the entire study.

+B: Exposures

Patients were identified who had a colorectal cancer diagnosis in the CPRD and HES data (ICD-10 sections C18–20, excluding C18.1 Appendix). The non-malignant diagnoses were confirmed from the ICD-10 discharge codes associated with the admission, including inflammatory bowel disease (*Appendix S1*, supporting information), diverticular disease (*Appendix S1*) and other. Co-morbidity was determined from the CPRD and classified using the Charlson index before admission for surgery[19]. Admission type was defined as elective or emergency, based on the type of admission recorded for the surgical procedure. Smoking status was classified as never, ever, current or missing, based on CPRD smoking records before the operation. Body mass index (BMI) was recorded from CPRD records, and patients were classified as having a BMI of less than 30 kg/m^2, 30 kg/m^2 or more, or missing data. Laparoscopic surgery was defined as any surgery accompanied by a laparoscopic code. Prescriptions for the oral contraceptive pill and hormone replacement therapy (HRT) were identified from the CPRD, and users were classified as current if the prescription was within 3 months of the index operation.

+B: Outcome definition

VTE diagnosis was determined from medical codes in the CPRD and HES. These were considered to indicate a valid VTE event if supported by either: a prescription for an anticoagulant or other evidence of treatment in an anticoagulation clinic (such as a medical code) between 15 days before and 90 days after the VTE diagnosis, or a date of death within 30 days of the event. Additionally, an underlying cause of death of VTE was included as evidence of a VTE diagnosis. The definition using primary care data alone has been validated previously[20] and used in the authors' previous studies of VTE[21,22].

+B: Statistical analysis

The date of diagnosis of VTE was taken to be the episode start date for VTEs occurring within the same hospital admission as the index operation. Absolute rates of VTE (per 1000 person-years) were calculated by dividing the number of individuals with VTE by the person-time at risk for the first year of follow-up after operation. This was done overall and then separately for each exposure of interest. Patients with missing data were analysed as a separate category, and rates and risk were presented separately for them. A Cox proportional hazards model was then created to include all exposures, to estimate hazard ratios (HRs) and 95 per cent c.i. The risk of VTE was then evaluated by indication for surgery and type of admission, adjusting for age and co-morbidity. A female-only analysis was performed in order to account for current use (within 3 months of surgery) of the oral contraceptive pill or HRT, given their known association with an increased risk of VTE[23]. Age was fitted as an interaction term in the models using likelihood ratio tests to look for the presence of a significant interaction. A further analysis was undertaken of the rates of VTE by calendar month after surgery in order to define the period of greatest risk up to 12 weeks. A sensitivity analysis was performed of all patients from the date of hospital discharge, excluding patients who had an in-hospital VTE, to determine the rates of VTE after discharge. All data

management and analyses were performed using Stata$^{®}$ version 12 (StataCorp, College Station, Texas, USA).

+A: Results

In total, 12 388 patients had a colectomy and 312 (2.5 per cent) developed VTE in the first year after surgery. The proportion of men and women undergoing emergency surgery was similar; however, in the elective setting the proportion of women who had surgery for non-malignant was greater than that for malignant disease (56.4 *versus* 45.2 per cent; $P < 0.001$, χ^2 test) (*Table 1*). Patients undergoing surgery for non-malignant disease were younger than those undergoing surgery for malignant disease (median (i.q.r.) 62 (46–74) *versus* 72 (64–79) years respectively; $P = 0.001$, Kruskal–Wallis test). Patients undergoing emergency or elective surgery for malignant disease were more likely to be ever or current smokers than those with non-malignant disease (*Table 1*) ($P < 0.001$, χ^2 test). In total, 12.5 per cent of the patients (1547 of 12 388) had a laparoscopic procedure during the study interval, increasing to 33.7 per cent (302 of 895) in the final year of the study.

In the emergency setting, 1750 (44.4 per cent) of 3938 patients had surgery for malignant disease; of those undergoing surgery for non-malignant disease, 502 (22.9 per cent) of 2188 were for inflammatory bowel disease (IBD) and 651 (30.0 per cent) of 2188 were for diverticular disease, with the remainder for other indications. In the elective setting 6559 (77.6 per cent) of 8450 patients underwent surgery for malignant disease; of those having surgery for non-malignant disease 527 (27.9 per cent) were for IBD and 579 (30.6 per cent) for diverticular disease, with the remainder for other indications.

+B: Venous thromboembolism rates overall, by admission type and indication

The overall rate of VTE following colectomy for any indication was 29.59 (95 per cent c.i. 26.48 to 33.06) per 1000 person-years at 1 year. The rate of VTE was highest in the first month after emergency surgery, and declined from 121.68 per 1000 person-years in the first month to 25.65 per 1000 person-years during the rest of the follow-up interval. The overall rate was 2.2-fold higher (adjusted HR 2.23, 95 per cent c.i. 1.76 to 2.50) for emergency compared with elective admissions (crude rate 39.44 *versus* 25.78 per 1000 person-years respectively) in the year after surgery. For malignant disease, rates of VTE were 2.8-fold higher (adjusted HR 2.84, 2.04 to 3.94) than for non-malignant disease (36.85 *versus* 14.56 per 1000 person-years respectively). When patients in the non-malignant group without a clear indication for surgery were excluded, there was little difference in the absolute rates (14.56 *versus* 10.94 per 1000 person-years, including and excluding patients without a clear indication respectively).

Laparoscopic surgery was not associated with a reduction in risk of VTE in the first year after surgery (unadjusted HR 0.91, 95 per cent c.i. 0.65 to 1.28). For women, the overall rate of VTE was 2.3-fold higher (adjusted HR 2.23, 1.59 to 3.13) for emergency compared with elective admissions in the year after surgery. When further adjustment was made for current use of either HRT or the oral contraceptive pill this association did not change (adjusted HR 2.24, 1.60 to 3.14); thus, no adjustment for these variables was made in subsequent analyses.

+B: *Overall rates of venous thromboembolism*

+C: Elective colectomy

Patients who had elective colectomy for non-malignant disease had the lowest crude rate of VTE (6.31 per 1000 person-years) (*Table 2*). The crude rate of VTE following elective colectomy increased with increasing age, peaking in those aged over 60 years (36.33 per

1000 person-years). The risk of VTE increased with increasing age, although the effects of age were attenuated when accounting for indication, suggesting an interaction between age and indication (*P* < 0.005, likelihood ratio test). When stratified by indication, the risk of VTE by age increased for patients with a non-malignant indication, peaking in those over 80 years old (crude rate 20.80 per 1000 person-years), but there was no increase in patients with a malignant indication.

+C: Emergency colectomy

Patients undergoing an emergency colectomy for malignant disease had a 2.4-fold increase in risk of VTE in the year following colectomy compared with those with a non-malignant indication (*Table 3*). The risk of VTE increased with increasing age, but the effects of age were attenuated when accounting for indication, suggesting an interaction between age and indication (*P* < 0.001, likelihood ratio test). When stratified by indication, the risk of VTE by age increased for patients with a non-malignant indication, peaking in those over the age of 60 years (crude rate 37.62 per 1000 person-years), but there was no increase in patients with a malignant indication.

+B: Rates in first month after surgery

+C: Elective surgery

Patients who had an elective colectomy for malignant disease had a 3.8-fold increased risk of VTE in the first month after surgery *versus* patients with non-malignant disease (HR 3.81, 95 per cent c.i. 0.90 to 15.99), although this was not significant (*Table 4*). The absolute rate of VTE in all patients fell after the first postoperative month (*Fig. 1*).

+C: Emergency surgery

Patients undergoing emergency colectomy had a similar cumulative incidence of VTE in the first month after surgery regardless of indication, with a higher absolute rate in those with a malignant indication: 120.98 per 1000 person-years *versus* 114.76 per 1000 person-years in those with non-malignant disease (HR 1.12, 95 per cent c.i. 0.56 to 2.27) (*Table 4* and *Fig. 2*).

The rate of VTE following a non-malignant emergency colectomy was 2.0-fold greater than that for an elective colectomy with a malignant indication in the first month after surgery (absolute rate 114.76 *versus* 61.83 per 1000 person-years respectively; HR 2.04, 95 per cent c.i. 1.13 to 3.74). Following the first month after surgery, the absolute rate of VTE in all patients fell during the remainder of the year but remained highest in those undergoing emergency surgery for malignant disease (54.42 per 1000 person-years) (*Table 4*).

+B: Sensitivity analysis after discharge from hospital

+C: Elective surgery

In the first month after hospital discharge the absolute rates of VTE were similar to those in the first month after surgery (non-malignant: 13.18 *versus* 12.98 per 1000 person-years; malignant: 68.76 *versus* 61.83 per 1000 person-years) (*Tables 4* and *5*).

+C: Emergency surgery

In the first month after discharge from hospital the absolute rate of VTE was lower following emergency admission for non-malignant disease compared with that in the first month after surgery (78.01 *versus* 114.76 per 1000 person-years). A reduction was also seen in the month following discharge in patients with a malignant indication: 106.38 per 1000 person-years *versus* 120.98 per 1000 person-years in the first month after surgery (*Tables 4* and *5*).

+A: Discussion

This study found an overall 1-year incidence of VTE following colectomy of 2.5 per cent. The highest overall absolute rates of VTE occurred after emergency surgery for malignant disease, and rates increased with age for non-malignant indications, although not in patients with cancer. Undoubtedly, the period of greatest risk for VTE following colectomy is the first month after surgery: around 0.5 per cent by the end of this period following any colectomy, and 1.0 per cent with an emergency admission. Of particular note is the fact that patients undergoing emergency colectomy for either a malignant or a non-malignant indication had similar high rates of VTE in the early postoperative period. Given that current guidance recommends extending VTE prophylaxis following colectomy for malignancy to 28 days after surgery, randomized clinical trials of the benefits of extended prophylaxis may be warranted in those patients having an emergency colectomy for non-malignant disease.

This study used linked data to identify patients undergoing colectomy from population-based data, with identification of operative procedures from secondary care along with defining VTE in a validated manner from primary[20] and secondary care, and is thus uniquely placed to quantify VTE risk accurately. The identification of VTE following discharge from hospital relies on clinical suspicion of the general practitioner and subsequent referral for investigation, thereby minimizing the surveillance bias that may occur in patients identified solely in hospital, as has been suggested in other studies[24]. The indication for surgery in patients with non-malignant disease was not classified specifically in 25.2 per cent of patients (1029 of 4079) and this figure is in keeping with data previously published using stand-alone HES data[25]. Furthermore, when these patients were excluded from the analysis, the absolute rates of VTE remained broadly similar, suggesting that the risk of VTE in these patients was no greater than that of patients with a clear indication for surgery. Although the authors were unable to identify patients who received thromboprophylaxis at or around the time of surgery during the study interval (2001–2011), only in the last year of the study were there

recommendations for prolonged thromboprophylaxis following surgery in the UK. Uptake of this by colorectal surgeons at this time was poor[26], so patients would at most have received low molecular weight heparin while an inpatient following surgery[15].

The sensitivity analysis of patients following discharge demonstrates that patients were still at increased risk of VTE after discharge, regardless of whether they had received thromboprophylaxis in hospital. In addition, rates of thromboprophylaxis at this time were low, with the ENDORSE study[27] estimating that only 50 per cent of patients received appropriate thromboprophylaxis, with a lower proportion in those undergoing emergency surgery – in whom the present study found the highest absolute rates of VTE. Nevertheless the possibility cannot be excluded that rates of VTE might have been higher in some groups than was observed in this study, precisely because they received longer prophylaxis.

The potential effects of laparoscopic resection on the rates of VTE could not be assessed fully. Laparoscopic resection rates reported here were low, as it was during the study period that laparoscopic resection rates began to increase. The finding of approximately one-third of resections being performed laparoscopically by the end of the study is in keeping with data from the National Bowel Cancer Audit[28]. Further studies are required to assess the potential benefits of laparoscopic surgery in this group of patients.

Rates of VTE following a diagnosis of colorectal cancer were recently the subject of a systematic review and meta-analysis[29], which reported an overall incidence of 16 per 1000 person-years based on four studies reporting incidence in average-risk populations. Few studies have, however, described the risk of VTE following surgery for malignant disease, with conflicting results being reported based on the comparison population used. Two population-based studies[14,30] reporting on VTE risk following a diagnosis of colorectal cancer found a decreased risk of VTE after surgery; however, the comparison group comprised

patients who did not have surgery because of advanced disease or significant co-morbidity, who have the greatest risk of VTE. Alcalay and colleagues[14] reported a 6-month rate of VTE after surgery of 40 per 1000 patient-years, which is similar to the present 6-month rate of 48.08 (95 per cent c.i. 41.57 to 55.62) per 1000 person-years. Their study, however, did not report rates by emergency or elective resection. A study[13] using data from the American College of Surgeons National Surgery Quality Improvement Program National Surgery Quality Improvement Program (NSQIP) database reported an overall 30-day VTE rate of 2.0 per cent (446 of 21943) following colectomy for colorectal cancer, but gave limited information on timing after surgery as follow-up was limited to 30 days, and did not report rates by emergency and elective resections. A further study[31] using NSQIP data from 2005 to 2008 reported an overall VTE rate of 2.5 per cent following colectomy, with a postdischarge rate of 0.7 per cent, which is in keeping with the 0.5 per cent rate found in the present study for all patients following colectomy. Fleming and co-workers[31] found no difference in VTE rates between non-malignant and malignant disease (both 0.7 per cent), although they did not report rates according to whether surgery was performed as an emergency or electively. The present study, however, has shown a clear increased risk for malignant disease, of 2.4-fold in the first year after emergency surgery and 4.2-fold following elective surgery.

Few studies have reported the risk of VTE after surgery for non-malignant disease. A study[12] using data from the NSQIP database reported a 30-day risk of VTE following surgery for IBD of 2.3 per cent (242 of 10 431). This is higher than the 30-day rate for non-malignant disease in the present study; however, it is not clear whether Wallaert et al.[12] excluded patients who had had a VTE previously, as in the present study. Their study did, however, find that emergency surgery resulted in a 1.8-fold (odds ratio 1.8, 95 per cent c.i. 1.2 to 2.6) increase in risk of VTE compared with elective surgery. Sweetland and colleagues[32] reported an increased VTE risk in women undergoing gastrointestinal surgery (relative risk 56.0, 95

per cent c.i. 39.4 to 80.4) and cancer surgery (relative risk 91.6, 73.9 to 113.4) compared with the risk in women who did not have surgery, with the greatest risk in the first 6 weeks after operation. These authors were, however, unable to describe the risk in detail according to the timing of surgery (emergency or elective), or indication for surgery in terms of non-malignant and malignant disease.

Current guidance from the National Institute for Health and Care Excellence[15] and the American College of Chest Physicians[33] suggests that patients undergoing colectomy for malignant disease should receive 28 days (4 weeks) of extended pharmacological prophylaxis after surgery. This guidance is supported by the present findings, which indicate an increased risk of VTE in patients undergoing surgery for malignant disease in both the elective and emergency setting that extends beyond the inpatient period. However, the present results also indicate that patients having emergency surgery for non-malignant disease have a similar increased risk of VTE during the 30 days after surgery to that of patients with malignant disease operated on as an emergency. Indeed, the magnitude of the risk in patients undergoing emergency non-malignant colectomy was greater than that of patients undergoing colectomy for malignant disease in the elective setting, who currently receive extended prophylaxis. Given the findings of the ENDORSE study[27], every effort should be made to assess risk in these patients before operation and ensure that appropriate thromboprophylaxis is prescribed during their hospital stay. Interventional studies assessing the benefit and risks of extended prophylaxis in patients undergoing emergency colectomy for non-malignant disease may be warranted.

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Supporting information

Additional supporting information may be found in the online version of this article:

Appendix S1 OPCS and ICD codes used to identify colectomy, inflammatory bowel disease and diverticular disease (Word document)

Fig. 1 Cumulative incidence of venous thromboembolism (VTE) following elective admission by indication for surgery
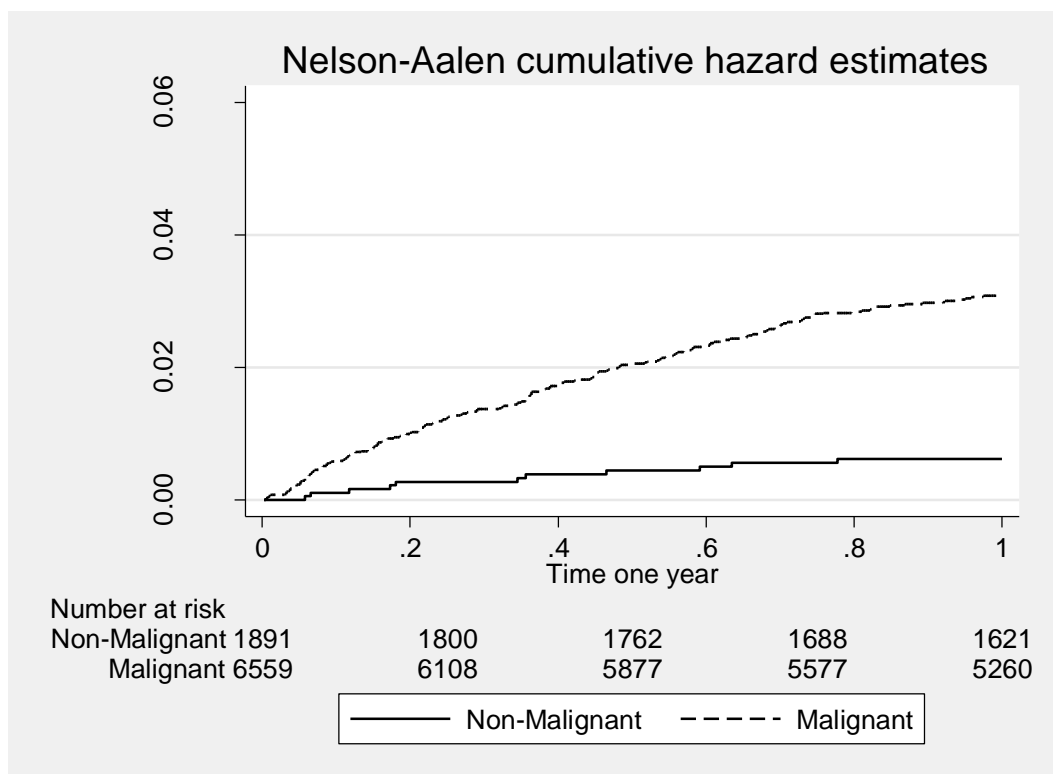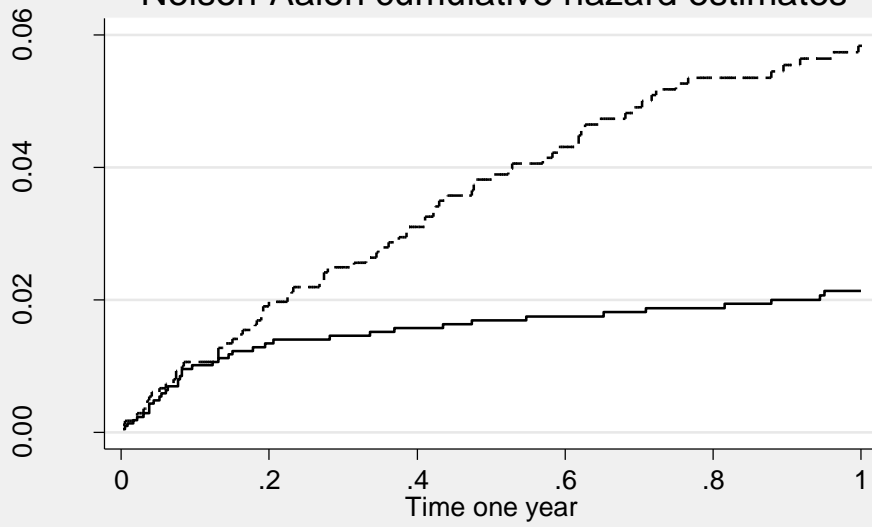

Fig. 2 Cumulative incidence of venous thromboembolism (VTE) following emergency admission by indication for surgery

Nelson-Aalen cumulative hazard estimates

Number at risk

Non-Malignant	2188	1749	1664	1592	1515
Malignant	1750	1363	1232	1116	1022

—— Non-Malignant ----- Malignant

Table 1 Demographics of colectomy cohort, by admission type and indication for surgery

	Emergency (n = 3938)		Elective (n = 8450)	
	Non-malignant (n = 2188)	Malignant (n = 1750)	Non-malignant (n = 1891)	Malignant (n = 6559)
Age (years)				
< 40	389 (17.8)	33 (1.9)	362 (19.1)	57 (0.9)
40–49	218 (10.0)	72 (4.1)	218 (11.5)	212 (3.2)
50–59	310 (14.2)	177 (10.1)	318 (16.8)	767 (11.7)
60–69	409 (18.7)	356 (20.3)	459 (24.3)	1774 (27.0)
70–79	502 (22.9)	579 (33.1)	373 (19.7)	2329 (35.5)
80–89	360 (16.5)	533 (30.5)	161 (8.5)	1420 (21.6)
Sex				
M	985 (45.0)	825 (47.1)	824 (43.6)	3598 (54.9)
F	1203 (55.0)	925 (52.9)	1067 (56.4)	2961 (45.1)
No. of co-morbidities				
0	1120 (51.2)	739 (42.2)	1058 (55.9)	2136 (32.6)
1	466 (21.3)	327 (18.7)	401 (21.2)	880 (13.4)
2	285 (13.0)	323 (18.5)	240 (12.7)	1848 (28.2)
≥ 3	317 (14.5)	361 (20.6)	192 (10.2)	1695 (25.8)
Body mass index (kg/m^2)				
< 30	1356 (62.0)	1140 (65.1)	1253 (66.3)	4370 (66.6)
≥ 0	377 (17.2)	300 (17.1)	354 (18.7)	1370 (20.9)
Missing	455 (20.8)	310 (17.7)	284 (15.0)	819 (12.5)
Smoking status				
Never	517 (23.6)	274 (15.7)	405 (21.4)	730 (11.1)
Ever	887 (40.5)	861 (49.2)	853 (45.1)	3322 (50.6)
Current	563 (25.7)	487 (27.8)	523 (27.7)	2209 (33.7)
Missing	221 (10.1)	128 (7.3)	110 (5.8)	298 (4.5)

Table 2 Rates of venous thromboembolism for elective admission, by indication, age, co-morbidity using the Charlson index, body mass index and smoking

	Rate per 1000 person-years	Unadjusted HR	Adjusted HR*
Indication			
Non-malignant	6.31 (3.49, 11.37)	1.00 (reference)	1.00 (reference)
Malignant	31.59 (27.35, 36.49)	4.03 (2.20, 7.41)	4.16 (2.24, 7.72)
Age (years)			
< 40	–	–	–
40–49	9.79 (3.67, 26.07)	1.00 (reference)	1.00 (reference)
50–59	21.85 (14.39, 33.18)	2.22 (0.77, 6.45)	1.76 (0.61, 5.13)
60–69	36.33 (28.93, 45.63)	3.69 (1.35, 10.08)	2.67 (0.97, 7.37)
70–79	27.91 (21.96, 35.45)	2.02 (1.03, 7.75)	1.98 (0.72, 5.50)
> 80	21.37 (14.85, 30.75)	1.44 (0.76, 6.12)	1.56 (0.54, 4.50)
No. of co-morbidities			
0	25.08 (19.94, 31.55)	1.00 (reference)	1.00 (reference)
1	27.76 (19.63, 39.25)	1.06 (0.70, 1.61)	1.04 (0.68, 1.59)
2	26.48 (20.07, 34.93)	0.96 (0.67, 1.38)	0.81 (0.56, 1.16)
3	24.83 (18.29, 33.73)	0.89 (0.61, 1.30)	0.72 (0.48, 1.07)
Body mass index (kg/m^2)			
< 30	21.45 (17.78, 25.88)	1.00 (reference)	1.00 (reference)
≥ 30	41.49 (32.48, 53.01)	1.88 (1.38, 2.56)	1.84 (1.34, 2.51)
Missing	23.49 (15.61, 35.34)	1.17 (0.74, 1.83)	1.20 (0.73, 1.95)
Smoking status			
Never	18.84 (12.02, 29.54)	1.00 (reference)	1.00 (reference)
Ever	26.72 (21.99, 32.47)	1.36 (0.83, 2.22)	1.19 (0.73, 1.96)
Current	28.2 (22.27, 35.70)	1.39 (0.84, 2.31)	1.18 (0.71, 1.98)
Missing	19.04 (9.08, 39.93)	1.08 (0.45, 2.56)	0.92 (0.37, 2.32)

Values in parentheses are 95 per cent c.i. *Adjusted for all other variables in the table. HR, hazard ratio.

Table 3 Rates of venous thromboembolism for emergency admission, by indication, age, co-morbidity using the Charlson index, body mass index and smoking

	Rate per 1000 person-years	Unadjusted HR	Adjusted HR*
Indication			
Non-malignant	23.1 (16.88, 31.62)	1.00 (reference)	1.00 (reference)
Malignant	61.44 (49.14, 76.82)	2.59 (1.76, 3.80)	2.42 (1.61, 3.65)
Age (years)			
< 40	16.04 (7.21, 35.71)	1.00 (reference)	1.00 (reference)
40–49	30.44 (15.22, 60.87)	1.91 (0.66, 5.51)	1.48 (0.51, 4.30)
50–59	24.3 (13.07, 45.15)	1.51 (0.55, 4.15)	1.03 (0.37, 2.88)
60–69	54.98 (39.09, 77.34)	3.35 (1.40, 8.00)	2.06 (0.83, 5.09)
70–79	60.19 (45.08, 80.36)	3.61 (1.54, 8.46)	2.14 (0.87, 5.28)
> 80	24.6 (14.28, 42.36)	1.44 (0.55, 3.79)	0.83 (0.30, 2.32)
No. of co-morbidities			
0	42.13 (32.85, 54.04)	1.00 (reference)	1.00 (reference)
1	33.36 (21.52, 51.71)	0.79 (0.48, 1.31)	0.76 (0.45, 1.27)
2	29.17 (16.94, 50.23)	0.68 (0.38, 1.24)	0.52 (0.28, 0.95)
≥ 3	49.45 (32.24, 75.84)	1.12 (0.68, 1.84)	0.85 (0.51, 1.43)
Body mass index (kg/m^2)			
< 30	36.84 (29.10, 46.64)	1.00 (reference)	1.00 (reference)
≥ 30	64.71 (46.00, 91.02)	1.75 (1.15, 2.65)	1.70 (1.11, 2.60)
Missing	25.07 (14.85, 42.33)	0.67 (0.38, 1.19)	0.83 (0.43, 1.62)
Smoking status			
Never	28.51 (17.72, 45.85)	1.00 (reference)	1.00 (reference)
Ever	46.16 (35.92, 59.33)	1.60 (0.94, 2.75)	1.39 (0.80, 2.41)
Current	42.89 (30.49, 47.27)	1.49 (0.83, 2.68)	1.24 (0.68, 2.26)
Missing	19.67 (8.19, 47.27)	0.68 (0.25, 1.83)	0.83 (0.27, 2.55)

Values in parentheses are 95 per cent c.i. *Adjusted for all other variables in the table. HR, hazard ratio.

Table 4 Rates of venous thromboembolism in the first month after surgery, by admission type and indication

	Rate (per 1000 person-years)		
	First month after surgery	Time from first month to 1 year	Adjusted HR*
Elective			
Non-malignant	12.98 (3.25, 51.89)	5.65 (2.94, 10.86)	1.00 (reference)
Malignant	61.83 (43.96, 86.98)	28.56 (24.36, 33.48)	3.81 (0.90, 15.99)
Emergency			
Non-malignant	114.76 (73.20, 179.91)	13.13 (8.47, 20.36)	1.00 (reference)
Malignant	120.98 (74.12, 197.48)	54.42 (42.34, 69.94)	1.12 (0.56, 2.27)

Values in parentheses are 95 per cent c.i. *Cox regression analysis adjusted for age and sex. HR, hazard ratio.

Table 5 Rates of venous thromboembolism in the first month after discharge from hospital, by admission type and indication

	Rate in first month after hospital discharge (per 1000 person-years)
Elective	
Non-malignant	13.18 (3.29, 52.71)
Malignant	68.76 (49.61, 95.33)
Emergency	
Non-malignant	78.01 (44.31, 137.36)
Malignant	106.38 (61.77, 183.21)

Values in parentheses are 95 per cent c.i.