Humes, D.J. and Walker, A.J. and Blackwell, J. and Hunt, B.J. and West, Joe (2015) Variation in the risk of venous thromboembolism following colectomy. British Journal of Surgery, 102 (13). pp. 1629-1638. ISSN 1365-2168

Access from the University of Nottingham repository:
http://eprints.nottingham.ac.uk/38809/1/BJS_mar_2016.pdf

Copyright and reuse:
The Nottingham ePrints service makes this work by researchers of the University of Nottingham available open access under the following conditions.

This article is made available under the University of Nottingham End User licence and may be reused according to the conditions of the licence. For more details see:
http://eprints.nottingham.ac.uk/end_user_agreement.pdf

A note on versions:
The version presented here may differ from the published version or from the version of record. If you wish to cite this item you are advised to consult the publisher's version. Please see the repository url above for details on accessing the published version and note that access may require a subscription.

For more information, please contact eprints@nottingham.ac.uk
Variation in the risk of venous thromboembolism following colectomy

D. J. Humes¹,², A. J. Walker¹, J. Blackwell¹, B. J. Hunt³ and J. West¹

¹Division of Epidemiology and Public Health, School of Medicine, University of Nottingham, ²National Institute for Health Research Nottingham Digestive Disease Biomedical Research Unit, Nottingham University Hospitals NHS Trust and University of Nottingham, Nottingham, and ³Thrombosis and Haemophilia Centre, Guy’s and St Thomas’ NHS Foundation Trust, St Thomas’ Hospital, London, UK

Correspondence to: Mr D. J. Humes, Division of Epidemiology and Public Health, School of Community Health Sciences, University of Nottingham, Clinical Sciences Building 2, City Hospital, Nottingham NG5 1PB, UK (e-mail: david.humes@nottingham.ac.uk)

Presented to the Tripartite Colorectal Meeting, Birmingham, UK, June 2014; published in abstract form as Colorectal Dis 2014; 16(Suppl 2): 15

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 procedure1. 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\textsuperscript{2-5}. A subsequent systematic review\textsuperscript{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\textsuperscript{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\textsuperscript{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\textsuperscript{7,12}. Similarly, studies reporting the risk of VTE following colectomy for malignant disease have used a limited 30-day follow-up\textsuperscript{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\textsuperscript{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 \textit{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\textsuperscript{15}.

\textbf{+A: Methods}

The study was approved by the Independent Scientific Advisory Committee approval board (Protocol 11-051R).
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 review17 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 previously18 to be similar in terms of age, sex and geographical distribution to data from the UK population.

Cohort
The cohort was identified using OPCS codes for any colectomy from HES data between 2001 and 2011 (Appendix SI, 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 SI, supporting information), diverticular disease (Appendix SI) and other. Co-morbidity was determined from the CPRD and classified using the Charlson index before admission for surgery. 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/m², 30 kg/m² 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 and used in the authors’ previous studies of VTE.

+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. 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, \( \chi^2 \) 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) (\( P < 0.001 \), \( \chi^2 \) test). In total, 12.5 per cent of the patients (1547 of 12388) 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 \textit{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) \textit{(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 \textit{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) \textit{(Table 4)}.

\textit{+B: Sensitivity analysis after discharge from hospital}

\textit{+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 \textit{versus} 12.98 per 1000 person-years; malignant: 68.76 \textit{versus} 61.83 per 1000 person-years) \textit{(Tables 4 and 5)}.

\textit{+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 \textit{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 \textit{versus} 120.98 per 1000 person-years in the first month after surgery \textit{(Tables 4 and 5)}.

\textit{+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 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. 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. 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\textsuperscript{26}, so patients would at most have received low molecular weight heparin while an inpatient following surgery\textsuperscript{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\textsuperscript{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\textsuperscript{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\textsuperscript{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\textsuperscript{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\textsuperscript{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\textsuperscript{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\textsuperscript{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\textsuperscript{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\textsuperscript{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.\textsuperscript{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\textsuperscript{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\textsuperscript{15} and the American College of Chest Physicians\textsuperscript{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\textsuperscript{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.

+A: Acknowledgements

This work was funded by a National Institute for Health Research postdoctoral fellowship awarded to D.J.H. J.W. is funded by a University of Nottingham/Nottingham University
Hospitals NHS Trust Senior Clinical Research Fellowship. The funders had no role in the
design of the study, the collection, analysis and interpretation of data, the writing of the
article, or the decision to submit it for publication.

Disclosure: The authors declare no conflict of interest.

+A: References

1 <EPATH>Health and Social Care Information Centre. Hospital Episode Statistics.
   http://www.hscic.gov.uk/hes [accessed 28 July 2015].

2 Lausen I, Jensen R, Jorgensen LN, Rasmussen MS, Lyng KM, Andersen M et al.
   Incidence and prevention of deep venous thrombosis occurring late after general
   surgery: randomised controlled study of prolonged thromboprophylaxis. Eur J Surg
   1998; 164: 657–663.

3 Bergqvist D, Agnelli G, Cohen AT, Eldor A, Nilsson PE, Le Moigne-Amrani A et al.;
   ENOXACAN II Investigators. Duration of prophylaxis against venous
   thromboembolism with enoxaparin after surgery for cancer. N Engl J Med 2002; 346:
   975–980.

4 Rasmussen MS, Jorgensen LN, Wille-Jørgensen P, Nielsen JD, Horn A, Mohn AC
   et al., FAME Investigators. Prolonged prophylaxis with dalteparin to prevent late
   thromboembolic complications in patients undergoing major abdominal surgery: a
   multicenter randomized open-label study. J Thromb Haemost 2006; 4: 2384–2390.

5 Jørgensen LN, Lausen I, Rasmussen MS, Wille-Jørgensen P, Berqvist D. Prolonged
   thromboprophylaxis with low-molecular weight heparin following major general
   surgery: an individual patient data meta-analysis. Blood 2002; 100: Abstract 1952.
Rasmussen MS, Jørgensen LN, Wille-Jørgensen P. Prolonged thromboprophylaxis with low molecular weight heparin for abdominal or pelvic surgery. *Cochrane Database Syst Rev* 2009; (1) CD004318.

Shapiro R, Vogel JD, Kiran RP. Risk of postoperative venous thromboembolism after laparoscopic and open colorectal surgery: an additional benefit of the minimally invasive approach? *Dis Colon Rectum* 2011; **54**: 1496–1502.

Byrne BE, Mamidanna R, Vincent CA, Faiz O. Population-based cohort study comparing 30- and 90-day institutional mortality rates after colorectal surgery. *Br J Surg* 2013; **100**: 1810–1817.

Walker AJ, West J, Card TR, Humes DJ, Grainge MJ. Variation in the risk of venous thromboembolism in people with colorectal cancer: a population-based cohort study from England. *J Thromb Haemost* 2014; **12**: 641–649.

Strate LL, Erichsen R, Horváth–Puhó E, Pedersen L, Baron JA, Sørensen HT. Diverticular disease is associated with increased risk of subsequent arterial and venous thromboembolic events. *Clin Gastroenterol Hepatol* 2014; **12**: 1695–1701.

Van Assche G, Vermeire S, Rutgeerts P. Management of acute severe ulcerative colitis. *Gut* 2011; **60**: 130–133.

Wallaert JB, De Martino RR, Marsicovetere PS, Goodney PP, Finlayson SRG, Murray JJ *et al.* Venous thromboembolism after surgery for inflammatory bowel disease: are there modifiable risk factors? Data from ACS NSQIP. *Dis Colon Rectum* 2012; **55**: 1138–1144.

Davenport DL, Vargas HD, Kasten MW, Xenos ES. Timing and perioperative risk factors for in-hospital and post-discharge venous thromboembolism after colorectal cancer resection. *Clin Appl Thromb/Hemost* 2012; **18**: 569–575.
14 Alcalay A, Wun T, Khatri V, Chew HK, Harvey D, Zhou H et al. Venous thromboembolism in patients with colorectal cancer: incidence and effect on survival. J Clin Oncol 2006; 24: 1112–1118.

15 <B>National Institute for Health and Care Excellence (NICE). Venous Thromboembolism in Adults Admitted to Hospital – Reducing the Risk [CG92]. NICE: London, 2010.

16 Benson T. The history of the Read Codes: the inaugural James Read Memorial Lecture 2011. Inform Prim Care 2011; 19: 173–182.

17 Sinha S, Peach G, Poloniecki JD, Thompson MM, Holt PJ. Studies using English administrative data (Hospital Episode Statistics) to assess health-care outcomes – systematic review and recommendations for reporting. Eur J Public Health 2013; 23: 86–92.

18 <OTHER>Crooks C. Epidemiology of Upper Gastrointestinal Bleeding: Studying its Causes and Outcomes using Case Control Studies and Survival Analyses. PhD thesis, University of Nottingham, 2013.

19 Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987; 40: 373–383.

20 Lawrenson R, Todd JC, Leydon GM, Williams TJ, Farmer RD. Validation of the diagnosis of venous thromboembolism in general practice database studies. Br J Clin Pharmacol 2000; 49: 591–596.

21 Abdul Sultan A, Tata LJ, Grainge MJ, West J. The incidence of first venous thromboembolism in and around pregnancy using linked primary and secondary care data: a population based cohort study from England and comparative meta-analysis. PloS One 2013; 8: e70310.
22 Walker AJ, Card TR, West J, Crooks C, Grainge MJ. Incidence of venous thromboembolism in patients with cancer – a cohort study using linked United Kingdom databases. *Eur J Cancer* 2013; 49: 1404–1413.

23 Vinogradova Y, Coupland C, Hippisley-Cox J. Use of combined oral contraceptives and risk of venous thromboembolism: nested case–control studies using the QResearch and CPRD databases. *BMJ* 2015; 350: h2135.

24 Bilimoria KY, Chung J, Ju MH, Haut ER, Bentrem DJ, Ko CY *et al.* Evaluation of surveillance bias and the validity of the venous thromboembolism quality measure. *JAMA* 2013; 310: 1482–1489.

25 Faiz O, Warusavitarne J, Bottle A, Tekkis PP, Clark SK, Darzi AW *et al.* Nonelective excisional colorectal surgery in English National Health Service Trusts: a study of outcomes from Hospital Episode Statistics data between 1996 and 2007. *JAMA* 2010; 210: 390–401.

26 Srinivasaiah N, Arsalani-Zadeh R, Monson JR. Thrombo-prophylaxis in colorectal surgery: a National Questionnaire Survey of the members of the Association of Coloproctology of Great Britain and Ireland. *Colorectal Dis* 2012; 14: e390–e393.

27 Kakkar AK, Cohen AT, Tapson VF, Bergmann J-F, Goldhaber SZ, Deslandes B *et al.*; ENDORSE Investigators. Venous thromboembolism risk and prophylaxis in the acute care hospital setting (ENDORSE Survey): findings in surgical patients. *Ann Surg* 2010; 251: 330–338.

28 <EPATH>Health and Social Care Information Centre. *National Bowel Cancer Audit Annual Report 2013*. http://www.hscic.gov.uk/catalogue/PUB11105/nati-clin-audi-supp-prog-bowe-canc-2013-rep1.pdf [accessed 28 July 2015].

29 Horsted F, West J, Grainge MJ. Risk of venous thromboembolism in patients with cancer: a systematic review and meta-analysis. *PLoS Med* 2012; 9: e1001275.
30 Choi S, Lee KW, Bang SM, Kim S, Lee JO, Kim YJ et al. Different characteristics and prognostic impact of deep-vein thrombosis/pulmonary embolism and intraabdominal venous thrombosis in colorectal cancer patients. *Thromb Haemost* 2011; 106: 1084–1094.

31 Fleming FJ, Kim MJ, Salloum RM, Young KC, Monson JR. How much do we need to worry about venous thromboembolism after hospital discharge? A study of colorectal surgery patients using the National Surgical Quality Improvement Program database. *Dis Colon Rectum* 2010; 53: 1355–1360.

32 Sweetland S, Green J, Liu B, Berrington de González A, Canonico M, Reeves G et al.; Million Women Study collaborators. Duration and magnitude of the postoperative risk of venous thromboembolism in middle aged women: prospective cohort study. *BMJ* 2009; 339: b4583.

33 Gould MK, Garcia DA, Wren SM, Karanicolas PJ, Arcelus JI, Heit JA et al.; American College of Chest Physicians. Prevention of VYE in nonorthopedic surgical patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. *CHEST J* 2012; 141(Suppl): e227S–e277S.

**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

| Time one year | Non-Malignant | Malignant |
|---------------|---------------|-----------|
| 0             | 1749          | 1515      |
| 0.2           | 1664          | 1022      |
| 0.4           | 1592          |           |
| 0.6           | 1515          |           |
| 0.8           | 1515          |           |
| 1             | 1515          |           |

Number at risk
- Non-Malignant: 2,188
- Malignant: 1,750
Table 1 Demographics of colectomy cohort, by admission type and indication for surgery

| Age (years) | Emergency (n = 3938) | Elective (n = 8450) |
|-------------|----------------------|---------------------|
|             | Non-malignant (n = 2188) | Malignant (n = 1750) | Non-malignant (n = 1891) | Malignant (n = 6559) |
| < 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         | Emergency (n = 3938) | Elective (n = 8450) |
|-------------|----------------------|---------------------|
| 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 | Emergency (n = 3938) | Elective (n = 8450) |
|------------------------|----------------------|---------------------|
| 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/m²) | Emergency (n = 3938) | Elective (n = 8450) |
|-------------------------|----------------------|---------------------|
| < 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          | Emergency (n = 3938) | Elective (n = 8450) |
|-------------------------|----------------------|---------------------|
| 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

| Indication       | Rate per 1000 person-years | Unadjusted HR | Adjusted HR* |
|------------------|-----------------------------|---------------|--------------|
| 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/m²) |                  |               |              |
| < 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.
| Indication               | Rate per 1000 person-years | Unadjusted HR | Adjusted HR* |
|-------------------------|-----------------------------|---------------|--------------|
| 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/m²) |                             |               |              |
| < 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) |                  | Adjusted HR* |
|------------------|------------------------------|------------------|--------------|
|                  | First month after surgery    | Time from first month to 1 year |               |
| 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

| Admission Type | 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.