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## Venous thromboembolic complications to hysterectomy for benign disease

*a nationwide cohort study*

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*Published in:*  
Journal of Minimally Invasive Gynecology

*DOI (link to publication from Publisher):*  
[10.1016/j.jmig.2017.11.017](https://doi.org/10.1016/j.jmig.2017.11.017)

*Publication date:*  
2018

*Document Version*  
Version created as part of publication process; publisher's layout; not normally made publicly available

[Link to publication from Aalborg University](#)

*Citation for published version (APA):*  
Kahr, H. S., Thorlacius-Ussing, O., Christiansen, O. B., Skals, R. K., Torp-Pedersen, C., & Knudsen, A. (2018). Venous thromboembolic complications to hysterectomy for benign disease: a nationwide cohort study. *Journal of Minimally Invasive Gynecology*, 25(4), 715-723.e2. <https://doi.org/10.1016/j.jmig.2017.11.017>

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# Accepted Manuscript

Title: Venous Thromboembolic Complications to Hysterectomy for Benign Disease. a Nationwide Cohort Study

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PII: S1553-4650(17)31293-1  
DOI: <https://doi.org/10.1016/j.jmig.2017.11.017>  
Reference: JMIG 3355

To appear in: *The Journal of Minimally Invasive Gynecology*

Received date: 31-8-2017  
Revised date: 9-11-2017  
Accepted date: 24-11-2017

Please cite this article as: Henriette Strøm Kahr, Ole Thorlacius-Ussing, Ole Bjarne Christiansen, Regitze Kuhr Skals, Christian Torp-Pedersen, Aage Knudsen, Venous Thromboembolic Complications to Hysterectomy for Benign Disease. a Nationwide Cohort Study, *The Journal of Minimally Invasive Gynecology* (2017), <https://doi.org/10.1016/j.jmig.2017.11.017>.

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.



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2 **cohort study.**

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22  
23 **Source of the study**

24 A nationwide cohort study using The Danish National Patient Register.

25  
26 **Disclosure statements**

27 The authors have no conflicts of interests to declare. Henriette Strøm Kahr received financial  
28 support from Aalborg University, Department of Clinical Medicine and the Danish Cancer Research  
29 Fund during her Ph D study.

30  
31 **Prior Presentation**

32 This work has not been presented before.

33  
34 **Word count**

35 2,809 (Title page, abstract, précis and references not included)

36  
37 **Short title**

38 Venous thromboembolism after hysterectomy

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40  
41 **Précis**

42 The risk of venous thromboembolism after hysterectomy for benign disease is generally low,  
43 highest with an abdominal procedure, and particularly low after laparoscopic and vaginal  
44 procedures.

45

46 **Abstract**

47 Study Objective: To estimate the risk of venous thromboembolic complications following  
48 abdominal, laparoscopic and vaginal hysterectomy when performed for benign disorders.

49 Design: Nationwide cohort study (Canadian Task Force Classification II-2).

50 Setting: Data from Danish national registers on all women undergoing hysterectomy for benign  
51 conditions in the period 1996-2015.

52 Patients: Women aged 18 and above who underwent hysterectomy for benign disease were  
53 stratified into 3 groups according to hysterectomy approach: abdominal, laparoscopic or vaginal.

54 Intervention: Hysterectomy.

55 Measurements and Main Results: 89,931 women met the inclusion criteria. Venous  
56 thromboembolism (VTE) as a diagnosis or cause of death was identified. Risk of postoperative  
57 VTE was examined with Cox proportional hazard models adjusting for age, surgical approach and  
58 relevant comorbidities. Mean age was 49.9, 47.9 and 54.3 years for women with abdominal,  
59 laparoscopic and vaginal hysterectomy, respectively. Crude incidences of VTE within 30 days after  
60 hysterectomy were 0.24% (n=142), 0.13% (n=12) and 0.10% (n=21). The most important  
61 predictors of VTE were approach to hysterectomy and a history of thromboembolic disease. In the  
62 multivariable analysis risk of VTE was significantly reduced with laparoscopic hysterectomy (HR  
63 0.51; 95% CI 0.28-0.92,  $P=.03$ ) and vaginal hysterectomy (HR 0.39; 95% CI 0.24-0.63,  $P<.001$ )  
64 when compared to the abdominal procedure. Data on postoperative heparin thromboprophylaxis  
65 were available in 53,566 patients and adjusted HR was 0.63 (95 % CI 0.42-0.96,  $P=.03$ ) in patients  
66 receiving heparin thromboprophylaxis.

67 Conclusions: The 30-day cumulative incidence of VTE after hysterectomy for benign conditions  
68 was low overall (0.19%). Laparoscopic and vaginal hysterectomy carry a lower risk than the

69 abdominal procedure. Postoperative heparin thromboprophylaxis significantly reduces risk of VTE  
70 and should be considered especially if risk factors are present.

71

72 **Keywords:** Deep venous thrombosis; hysterectomy; pulmonary embolism; thromboprophylaxis.

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Accepted Manuscript

96 **Introduction**

97 Postoperative venous thromboembolism (VTE) is the second-most common medical complication  
98 to general surgery and results in excess morbidity and mortality[1]. The most feared consequence,  
99 pulmonary embolism (PE), is the most common preventable cause of hospital death[1]. Deep vein  
100 thrombosis (DVT) and PE are preventable with proper thromboprophylaxis as demonstrated in  
101 clinical trials[2].

102 One of the most common gynecologic procedures is hysterectomy with 400- 600,000 procedures  
103 per year in the United States[3,4]. Few studies have focused on the incidence of VTE in women  
104 undergoing hysterectomy for benign conditions. There are three different approaches to  
105 hysterectomy: abdominal, laparoscopic and vaginal. In 2015, 20 % were performed as abdominal,  
106 64 % as laparoscopic assisted (including robotic-assisted surgery) and 16 % as vaginal  
107 hysterectomies in Denmark[5]. The risk of postoperative DVT and PE, in patients undergoing  
108 surgery for benign conditions, is presumed to be low in general[6,7], and in particular when  
109 performed laparoscopically[8]. This is probably the reason, why pharmacologic VTE prophylaxis  
110 has not been used systematically. Despite being the recommendation in most clinical guidelines,  
111 the proportion of patients actually receiving thromboprophylaxis after hysterectomy may be as low  
112 as 11.9%[6]. Danish guidelines recommend postoperative venous thromboprophylaxis with low  
113 molecular weight heparin administered 4-12 hours following hysterectomy in prophylactic dose  
114 once daily until discharge from hospital, this can optionally be supplemented with graduated elastic  
115 compression stockings[9]. Few studies have focused on VTE in benign gynecologic surgery and  
116 recommendations on thromboprophylaxis have mostly been based on the experience from  
117 abdominal surgery and study populations with a broad variation of risk factors[10]. The striking  
118 difference between clinical practice and guidelines calls for a more precise estimation of risk of  
119 VTE after hysterectomy for benign conditions.

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## 123 **Materials and Methods**

### 124 **Data-sources**

125 This study is based on data from national Danish administrative registries.

126 In Denmark, every resident is at the time of birth or immigration assigned a unique and permanent  
127 civil registration number, which enables linkage between nationwide administrative registers on the  
128 individual level. The Danish National Patient Register (DNPR) was established in 1977 and holds  
129 data on all hospitalizations in Denmark[11]. Each admission is registered at discharge with one  
130 primary and if appropriate one or more secondary diagnoses according to the International  
131 Classification of Diseases, the 10<sup>th</sup> revision (ICD-10). Surgical procedures are registered according  
132 to the Nordic Medico-statistical Committee's Classification of Surgical Procedures[12], together  
133 with the indication for the procedure. There could be multiple indications for hysterectomy.

134 We retrieved information on hormone substitution and anticoagulant treatment from The Danish  
135 Register of Medicinal Product Statistics where all prescription based pharmacy dispensings are  
136 stored. The National Population Register and the National Causes of Death Register hold  
137 information on vital status, date of birth and death including cause of death.

### 138 **Study population**

139 All patients who underwent hysterectomy from January 1<sup>st</sup> 1996 until December 31<sup>st</sup> 2015 were  
140 identified. The patients were separated into three groups according to the surgical approach:

141 abdominal (subtotal or total abdominal hysterectomy comprised the codes KLCD00, KLCD96,  
142 KLCC10), laparoscopic (total, subtotal, vaginal and robotic assisted laparoscopic hysterectomy  
143 comprised the codes KLCD01, KLCD04, KLCC11, KLCD11, KLCD97) or vaginal (total or subtotal  
144 comprised the codes KLCD10, KLCC20, colpoperineoplasty and vaginal hysterectomy KLEF13).

145 Patients diagnosed with any type of cancer within 1 month prior to surgery or two months following  
146 the surgical procedure were excluded (ICD10 codes DC00-96). Radical hysterectomies (KLCD30,  
147 KLCD31, KLCD40) were excluded because these procedures are only performed in the case of  
148 gynecologic malignancy. We did not include hysterectomies performed at the same time as  
149 cesarean section or hysterectomy performed at the same time as cystectomy in the case of urine

150 bladder malignancy.

151 Patients were excluded if the specific date of surgery was not defined.

## 152 **Outcome**

153 VTE comprised the following ICD-10 codes: I80.1 (phlebitis or thrombophlebitis in the femoral  
154 vein), I80.2 (deep phlebitis or thrombophlebitis in other veins in lower extremities), I80.3 (deep  
155 phlebitis or thrombophlebitis in other veins in lower extremities without specification), I80.8  
156 (phlebitis or thrombophlebitis at other locations), I80.9 (phlebitis or thrombophlebitis without  
157 specification) and I26 (pulmonary embolism). If one of these codes occurred prior to the date of  
158 hysterectomy it was registered as a previous VTE. If the code was assigned to a patient within one  
159 month after hysterectomy it was registered as a postoperative VTE.

## 160 **Confounders**

161 Use of hormones or antithrombotic agents prior to surgery was defined as at least one claimed  
162 prescription within 180 days before surgery of the following agents: oral contraceptives with  
163 estrogen in combination with progesterone (Anatomical Therapeutic Chemical Classification G03A,  
164 G03HB01) or hormone therapy (estrogen as monotherapy or in combination with progesterone,  
165 both orally and transdermal administrated G03F, G03CX, G03CA and G03CB; low dose estrogen  
166 vagitories were excluded by product number). Antithrombotic agents were defined including  
167 antiplatelet drugs (B01AC) and anticoagulant drugs (B01 except B01AC).

168 Co-morbidities were defined as one of the following ICD-10 codes if the code was used at  
169 discharge within 365 days prior to the hysterectomy date: ischemic heart disease (I20, I23, I24,  
170 I25), cerebral vascular disease (I60-69), acute myocardial infarction (I21), varices of the lower  
171 extremities (I83), thrombophilia (D68), heart failure ((I50), chronic obstructive lung disease (J44).

172 Two time periods were compared as the Danish Board of Health in 2003 published a national  
173 guideline for benign hysterectomy including recommendations on postoperative VTE prophylaxis  
174 with heparin injections and graduated elastic compression stockings during hospitalization[13]. A  
175 Danish national hysterectomy database was established in October 2003 and one of the clinical

176 indicators is the use of VTE prophylaxis which is registered in the DNPR by the clinicians  
177 (BOHA03C).  
178 Information on Body Mass Index (BMI) was obtained from the Danish Anesthesia Database (DAD).  
179 This information was not available for all patients since the database was established in 2004 and  
180 it does not cover all departments in Denmark.  
181 Data are reported in accordance with the STROBE statement[14].

182

### 183 **Statistics**

184 Cumulative incidence was calculated for the competing risks VTE and death after abdominal,  
185 laparoscopic and vaginal hysterectomy respectively. Time to event was calculated from the date of  
186 surgery, follow-up time was 30 days and data were analyzed using univariable and multivariable  
187 Cox proportional hazard regression. Hazard ratios (HRs) of VTE after abdominal, laparoscopic and  
188 vaginal hysterectomy were hence estimated and presented with 95% confidence intervals (95%  
189 CI). A *P*-value less than 0.05 was considered statistically significant. Plots of Schoenfeld Residuals  
190 were used to examine the proportional hazard assumption. Linearity between the continuous  
191 variable age and outcome was tested. Interaction between approach to hysterectomy and  
192 presence of uterine fibroids was tested using analysis of variance.  
193 Calculations were performed using SAS V.9.4 (SAS Institute, Cary, North Carolina, USA) and R  
194 version 3.1.0 (R Core Team (2014))[15].

195

### 196 **Ethics**

197 The study was approved by The Danish Data Protection Agency (Re: 2007-58-0015, int.ref: GEH-  
198 2010-001). Permission from the ethics committee is not required for retrospective register studies  
199 in Denmark.

200

### 201 **Results**

202 We identified 89,931 patients who underwent hysterectomy for benign conditions in the period  
203 January 1<sup>st</sup> 1996 until December 31<sup>st</sup> 2015. Patients were divided into three groups according to  
204 the route of hysterectomy: Abdominal (n=59,231), laparoscopic (n=9,198) and vaginal (n=21,502)  
205 (figure 1). Table 1 shows the demographic data of the cohort according to age at surgery, length of  
206 stay, body mass index (BMI), concomitant disease, use of medicine before surgery, the indication  
207 for hysterectomy and postoperative pharmacologic VTE prophylaxis. Women undergoing vaginal  
208 hysterectomy were older and more likely to have comorbidities, although the general incidence of  
209 comorbidity was low in the total cohort. The indication for hysterectomy was uterine prolapse in  
210 more than 50 % of cases within the vaginal hysterectomy group. In the abdominal and  
211 laparoscopic hysterectomy groups, uterine fibroids and abnormal uterine bleeding were the  
212 dominant causes.

213 Comparing the two time periods before and after January 1<sup>st</sup>, 2004 showed that the proportion of  
214 minimally invasive hysterectomy was increasing during the study period with 29,060 abdominal  
215 approaches in 36,365 hysterectomies before 2004 ~80 %. After January 1<sup>st</sup>, 2004 44 % of  
216 hysterectomies were performed as laparoscopic and vaginal procedures.

217 During 30-day follow up after surgery we observed 175 cases of VTE with 100 cases of PE. There  
218 were 109 deaths in the abdominal hysterectomy group compared to one in the laparoscopic and  
219 12 in the vaginal hysterectomy group.

220 Competing risk analysis of the cumulative incidence of VTE showed higher incidence with open  
221 surgery compared to the two minimally invasive methods. Cumulative incidence of mortality  
222 showed the highest incidence with open surgery compared to the two minimally invasive methods.  
223 (Figures S1 and S2 are provided in supplemental material).

224 Unadjusted HRs in different exposure groups are provided in table 2. The indication for  
225 hysterectomy could be strongly correlated to the choice of surgery approach as surgeons might  
226 prefer to perform abdominal hysterectomy in the presence of uterine and ovarian neoplasms.  
227 Statistical testing showed no evidence of interaction between hysterectomy approach and uterine  
228 fibroids ( $P=0.35$ ).

229 Length of stay was associated with surgical approach (table 1) with median value highest in the  
230 abdominal hysterectomy group and univariable analysis (table 2) shows that it is significantly  
231 associated with HR of VTE.  
232 Adjusting for age, time period, ovarian and uterine neoplasms, relevant drugs and concomitant  
233 disease, the laparoscopic (HR 0.51; 95% CI 0.28-0.92,  $P=.03$ ) and vaginal (HR 0.39; 95% CI 0.24-  
234 0.63,  $P<.001$ ) procedures are correlated with a significantly reduced HR of VTE when compared to  
235 abdominal hysterectomy (figure 2).  
236 The use of oral hormonal contraceptives or hormone therapy did not influence on the HR of VTE in  
237 women undergoing hysterectomy (figure 2 and 3). In contrast, anticoagulant drugs, previous acute  
238 myocardial infarction (AMI) and previous VTE significantly increase the HR of VTE (figure 2 and 3).  
239 Usage of postoperative heparin as VTE prophylaxis has been registered in the DNPR since 2004.  
240 There is no change in the impact of the different factors included in the first model (figure 2) when  
241 performing the same multivariable analysis on hysterectomies performed after 2003 including VTE  
242 prophylaxis instead of time period (figure 3). This subgroup analysis shows a reduced HR (0.63;  
243 95% CI 0.42-0.96,  $P=.03$ ) for VTE in patients receiving pharmacologic VTE prophylaxis.  
244 Data on BMI were available in 11,177 patients with overall mean BMI 26.1 (SD  $\pm 5.0$ ) and 19 VTE  
245 events (table 1). We found no difference in risk of VTE between BMI groups in a univariable Cox  
246 proportional hazard regression analysis. Because of the smaller number of events we did not  
247 attempt of multivariable analysis including BMI.

248

## 249 Discussion

250 This study demonstrates that the 30-day incidence of postoperative VTE after hysterectomy for  
251 any benign condition is low. The rate of VTE was lowest in patients treated with laparoscopic and  
252 vaginal hysterectomy compared to the abdominal approach.

253 A Cochrane review (2009) comparing the complication rates between different procedures  
254 concluded that vaginal hysterectomy was superior to abdominal on almost all outcome measures

255 and recommended laparoscopic surgery in cases where vaginal hysterectomy could not be  
256 performed[17]. However, there was no apparent difference in the VTE incidence according to  
257 surgical approach, probably due to limited power.

258 Barber et al (2014) found an overall incidence of VTE at 0.35 % in 44,167 women undergoing  
259 hysterectomy for benign conditions and showed abdominal hysterectomy to be associated with  
260 higher risk of VTE compared to minimally invasive surgery (OR 2.45; CI 1.77-3.40)[18]. Swenson  
261 et al (2015) registered 110 VTE events (0.5%) during 30 days of follow-up in 20,496 women with  
262 hysterectomy for benign, malignant and obstetric indications. Prominent risk factors were  
263 abdominal approach, cancer, BMI>35 and increased surgical time[19].

264 The frequency of VTE in these studies is consistent with our findings. The association between  
265 BMI and VTE is debated and experience from bariatric surgery suggests that it has been  
266 overestimated[20]. We found no association between BMI and VTE in a subgroup of the cohort;  
267 due to missing data, we could not include BMI in the multivariable analysis.

268 White et al (2003) showed, that the incidence of first-time VTE increases exponentially with age  
269 with a dramatically increase after the age of 60[21]. Ritch et al (2011) identified age as a significant  
270 risk factor of VTE after hysterectomy[6].

271 In accordance with these studies we found the crude HR of VTE increasing with age in the  
272 unadjusted model. This association could not be reproduced in the multivariable models, indicating  
273 a stronger association between VTE and approach to hysterectomy.

274 Several studies have reported an increased risk of VTE with hormone therapy (HT) [22]. In the  
275 present study we found no difference in HR between women on HT or oral contraceptives  
276 containing estrogen compared to women not exposed.

277 A benign pelvic mass might compress the iliac veins leading to venous stasis and subsequent  
278 thrombosis. Fletcher et al. (2009) found an increased risk of VTE (OR 3.75; CI 2.92-4.78,  $P<.001$ )  
279 among women with uterine fibroids with and without surgery when compared to the expected rate  
280 in hospitalized women[23]. Shiota et al. (2011) found an overall incidence of preoperative  
281 asymptomatic DVT at 3.7 % (31/843) in patients with benign ovarian tumors[24]. Our analysis

282 indicated no correlation between any benign indication for hysterectomy and risk of postoperative  
283 symptomatic VTE. Our dataset did not contain neoplastic size, therefore, the possible impact of  
284 large tumors on VTE risk cannot be assessed.

285 It must be emphasized that we can only report cases of symptomatic VTE's. The incidence would  
286 probably be higher with more sensitive methods as demonstrated in randomized controlled  
287 trials[2].

288 In Denmark, thromboprophylaxis is administered by the hospital and was not registered in the  
289 DNPR before 2004. Hansen et al. (2008) reported an increase in heparin thromboprophylaxis  
290 administered following hysterectomy from 20 % in 2004 to more than 90 % of patients undergoing  
291 hysterectomy for benign disease in 2006[25]. Surgeons were probably paying more attention to  
292 VTE prophylaxis after the establishment of the Danish Hysterectomy and Hysteroscopy Database  
293 and implementation of recommendations on postoperative VTE prophylaxis. Our results indicate a  
294 significant reduction in risk of VTE following hysterectomy for benign conditions when  
295 pharmacologic VTE prophylaxis was administered during hospital stay after surgery. The ACOG  
296 Practice Bulletin (2007) recommends initiation of venous thromboprophylaxis with graduated  
297 compression stockings or pneumatic compression devices before surgery as VTE begins in the  
298 perioperative period[10]. Our results show a decrease in HR of VTE in patients receiving  
299 postoperative heparin which is supported by Hansen et al. (2008) who found preoperative  
300 administration associated with higher risk of bleeding complications compared to postoperative  
301 administration and no apparent difference in risk of VTE.[26] From our study we cannot draw any  
302 conclusions on the timing of VTE prophylaxis. Not all patients received prophylaxis, it is likely that  
303 patients within a fast track regimen undergoing MIS are discharged before heparin administration.  
304 Increasing length of stay increased the HR of VTE in a univariable analysis (table 2), despite this  
305 finding we did not include it in the multivariable analysis as we believe the variable is not a  
306 confounder because it is on the causal pathway between main exposure and outcome[27]. Talec  
307 et al (2016) suggest individual evaluation of thromboprophylaxis in each patient based on patient-

308 related risk factors, type of surgery including length of operation and duration to mobilization[28].  
309 Our results support this approach to the planning of VTE prophylaxis.  
310 The strength of epidemiologic research using national registries is the availability of a large patient  
311 cohort. Through our study, we found an important association between the risk of VTE and the  
312 approaches to hysterectomy. Groups were considered highly comparable according to baseline  
313 characteristics. The vaginal approach was used more often in case of pelvic organ prolapse and  
314 the abdominal approach in the presence of benign neoplasms, consistent with available  
315 gynecologic guidelines[29,30]. Bias could arise from misclassification of diseases and treatments.  
316 We calculated cumulative incidence of VTE considering mortality as a competing risk to illustrate  
317 how mortality affect the probability of a VTE event to occur. As mortality was highest in the  
318 abdominal hysterectomy group we found no reason to think mortality precluded the occurrence of  
319 VTE in the laparoscopic and vaginal hysterectomy groups.  
320 The coding of co-morbidity and coexisting diseases in DNPR is validated by Thygesen et al.  
321 (2011), with a positive predictive value ranging from 82 to 100 %.[31]. The validity of VTE  
322 discharge diagnoses in DNPR was investigated by Severinsen et al. (2010) who found a positive  
323 predictive value of 75% for diagnoses coded at wards[32].  
324 Confounding by indication could arise if the indication for hysterectomy carries a risk of developing  
325 VTE. Most other studies included patients with both benign and malignant diseases[6,19]. We  
326 chose to exclude patients with malignant disease and also obstetric patients, as these conditions  
327 are recognized risk factors for VTE[33,34].

328

**329 Conclusion:**

330 The risk of postoperative VTE in the first 30 days after hysterectomy is low (0.19 %). Laparoscopic  
331 and vaginal approach to hysterectomy significantly reduce the risk of VTE when compared to  
332 abdominal approach and adjusted for age and relevant risk factors. Our results indicate that  
333 postsurgical use of pharmacologic thromboprophylaxis reduce the risk of VTE. If heparin  
334 prophylaxis is not routinely used we suggest individual evaluation in each patient considering

335 approach to surgery, concomitant disease and previous thromboembolic events.

336

### 337 **Acknowledgements**

338 Danish Anesthesia Database (DAD) is acknowledged.

339

340

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430 **Figure 1.** Flowchart presenting the patient selection using Danish National Registries.

431

432 **Figure 2.** Multivariable Cox proportional Hazards Regression analysis presenting hazard ratios of  
433 venous thromboembolism associated with the approach to hysterectomy, adjusted for age, time  
434 period, ovarian and uterine neoplasm, use of sex hormones, a history of acute myocardial  
435 infarction (AMI) and previous venous thromboembolism (VTE).

436 Abdominal hysterectomy is used as reference in the main exposure group, among categorical  
437 variables in the confounder group exposed individuals are compared to non-exposed.

438

439 **Figure 3.** Multivariable Cox proportional Hazards Regression analysis presenting hazard ratios of  
440 venous thromboembolism associated with the approach to hysterectomy, adjusted for age, use of  
441 postoperative thromboprophylaxis, ovarian and uterine neoplasm, use of sex hormones and a  
442 history of acute myocardial infarction (AMI) and previous venous thromboembolism (VTE).

443 Stratified for period, showing results after 2003. Abdominal hysterectomy is used as reference in  
444 the main exposure group, among categorical variables in the confounder group exposed  
445 individuals are compared to non-exposed.

446

447 **Figure S1.** Cumulative incidence of venous thromboembolism 30 days following hysterectomy.

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449 **Figure S2.** Cumulative incidence of death 30 days following hysterectomy.

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453 **Table 1. Baseline characteristics and variables related to treatment**

Variable*	Abdominal hysterectomy	Laparoscopic hysterectomy	Vaginal hysterectomy	Totals
	N=59,231	N=9,198	N=21,502	N=89,931
Mean age, years	49.9 ±10.4	47.9 ±10.5	54.3 ±13.2	50.7 ±11.3
Median length of stay, days (interquartile range)	3 (2,5)	1 (1,2)	2 (1,2)	3 (2,4)
Length of stay data missing	4	1	10	15
Body Mass Index (BMI)	26.2±5.2	25.7±5.3	25.9±4.7	26.1±5.0
BMI missing	52,706	8,394	17,654	78,754
Anticoagulant drugs	631 (1.1)	110 (1.2)	177 (0.8)	918 (1.0)
Antiplatelet drugs	2,243 (3.8)	359 (3.9)	1,633 (7.6)	4,235 (4.7)
Hormonal contraception	4,422 (7.5)	894 (9.7)	1,280 (6.0)	6,596 (7.3)
Hormone therapy	7,183 (12.1)	927 (10.1)	4,821 (22.4)	12,931 (14.4)
Hysterectomy before 2004	29,060 (49.1)	2,166 (23.5)	5,139 (23.9)	36,363 (40.4)
Hysterectomy after 2003	30,171 (50.9)	7,032 (76.5)	16,363 (76.1)	53,566 (59.6)
<b>Indication for hysterectomy<sup>†</sup></b>				
Abnormal uterine bleeding	21,187 (35.8)	4,389 (47.7)	7,806 (36.3)	33,382 (37.1)
Benign ovarian neoplasm	4,910 (8.3)	292 (3.2)	189 (0.9)	5,391 (6.0)
Uterine fibroids	34,849 (58.8)	3,314 (36.0)	4,888 (22.7)	43,051 (47.9)
Pelvic organ prolapse	1,209 (2.0)	319 (3.5)	10,935 (50.9)	12,463 (13.9)
Pelvic pain	8,536 (14.4)	2,061 (22.4)	3,115 (14.5)	13,712 (15.2)
Endometriosis	5,161 (8.7)	1,192 (13.0)	1,191 (5.5)	7,544 (8.4)
Cervical intraepithelial neoplasia	1,958 (3.3)	624 (6.8)	872 (4.1)	3,454 (3.8)
Endometrial hyperplasia	485 (0.8)	123 (1.3)	184 (0.9)	792 (0.9)
Urinary incontinence	628 (1.1)	66 (0.7)	588 (2.7)	1,282 (1.4)
Cancer predisposition	100 (0.2)	91 (1.0)	8 (0.04)	199 (0.2)
<b>Concomitant diseases</b>				
Ischemic heart disease	1,498 (2.5)	329 (3.6)	902 (4.2)	2,729 (3.0)
Cardiovascular disease	873 (1.5)	176 (1.9)	419 (1.9)	1,468 (1.6)
History of acute myocardial infarction	320 (0.5)	67 (0.7)	186 (0.9)	573 (0.6)
Thrombophilia	266 (0.4)	68 (0.7)	120 (0.6)	454 (0.5)
Varicose disease	1,838 (3.1)	350 (3.8)	1,166 (5.4)	3,354 (3.7)
Heart failure	345 (0.6)	53 (0.6)	158 (0.7)	556 (0.6)
Chronic obstructive lung disease	720 (1.2)	136 (1.5)	337 (1.6)	1,193

Venous thromboembolism after hysterectomy

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				(1.3)
Previous VTE	1,026 (1.7)	182 (2.0)	332 (1.5)	1,540 (1.7)
<b>Postoperative VTE prophylaxis<sup>‡</sup></b>	<b>N=30,171</b>	<b>N=7,032</b>	<b>N=16,363</b>	<b>N=53,566</b>
No prophylaxis	13,755 (45.6)	2,797 (39.8)	5,623 (34.4)	22,175 (41.4)
VTE prophylaxis	16,416 (54.4)	4,235 (60.2)	10,740 (65.6)	31,391 (58.6)

\* Data are expressed as N (column %), mean  $\pm$  SD.

† There could be more than one indication for hysterectomy.

‡ Only registered in patients undergoing surgery after 2003.

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459 **Table 2. Unadjusted hazard ratios (HRs) of venous thromboembolism (VTE) in**  
 460 **different exposure groups**

	-VTE events/N total	HR	95 % CI	P value
Age (by decade)	175/89,931	1.16	1.02-1.31	.019
Age<60 years	129/72,847	1.0 (reference)		
Age≥60 years	46/17,084	1.53	1.09-2.14	.013
Length of stay (LOS), days*	175/89,577	1.09	1.05-1.13	<.001
Abdominal hysterectomy	142/59,231	1.0 (reference)		
Laparoscopic hysterectomy	12/9,198	0.54	0.30-0.98	.042
Vaginal hysterectomy	21/21,502	0.41	0.26-0.64	<.001
Previous VTE	67/1,540	36.7	27.1-49.8	<.001
Previous acute myocardial infarction	6/573	5.7	2.5-12.8	<.001
Benign ovarian neoplasm	11/5,391	1.05	0.57-1.94	.867
Uterine fibroids	76/43,051	0.83	0.62-1.13	.834
Abnormal uterine bleeding	55/33,318	0.78	0.56-1.07	.117
Hormone therapy	24/12,931	0.95	0.62-1.46	.804
Contraceptives	13/6,596	1.01	0.58-1.78	.965
Anticoagulant drugs	31/918	21.5	14.6-31.7	<.001
<b>Surgery after 2003</b>				
After implementation of VTE prophylaxis	105/53,566	1.02	0.75-1.38	.907
VTE prophylaxis registered	43/31,391	0.49	0.33-0.72	<.001

461 \*354 patients with missing data on LOS or LOS exceeding follow-up time of 30 days were excluded from the  
 462 analysis. There were no cases of VTE within this group.  
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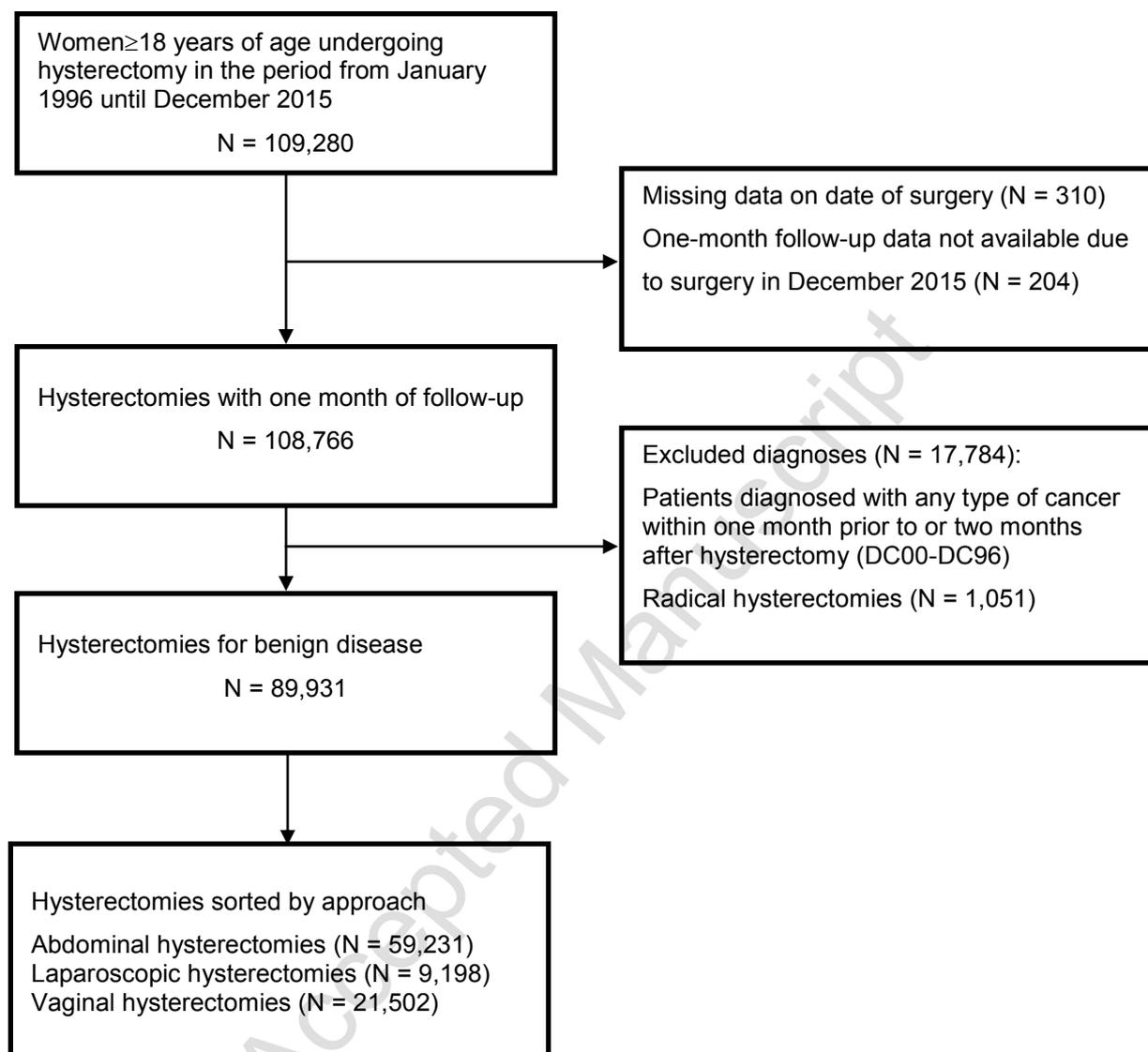
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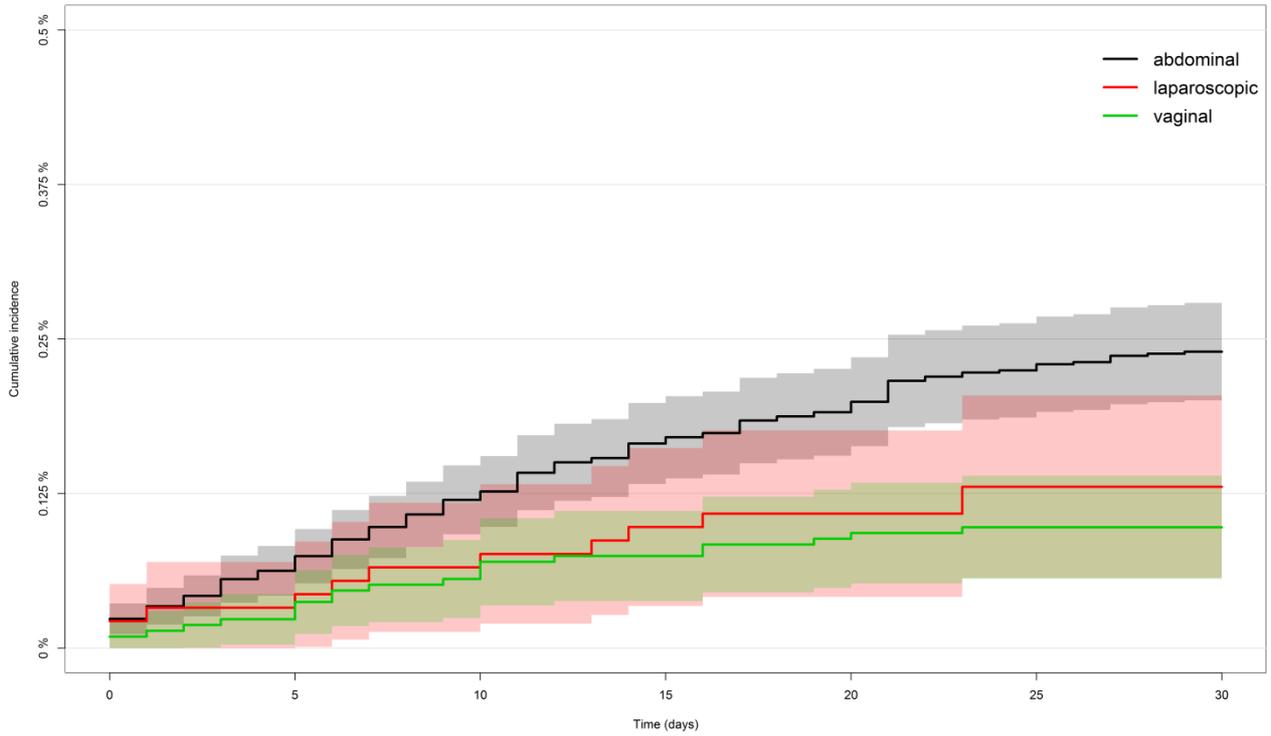
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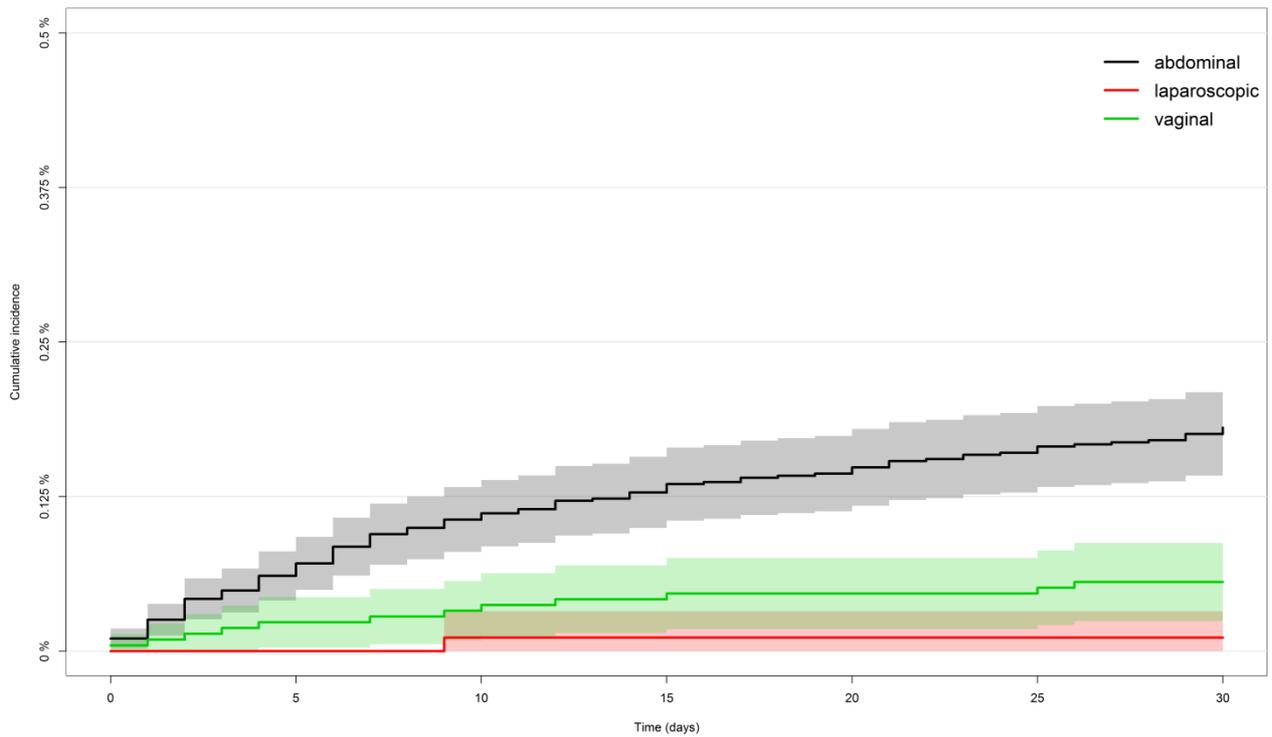


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