MOQC
MICHIGAN ONCOLOGY QUALITY CONSORTIUM

# Risk Calculator/ Bleeding Risk Factors

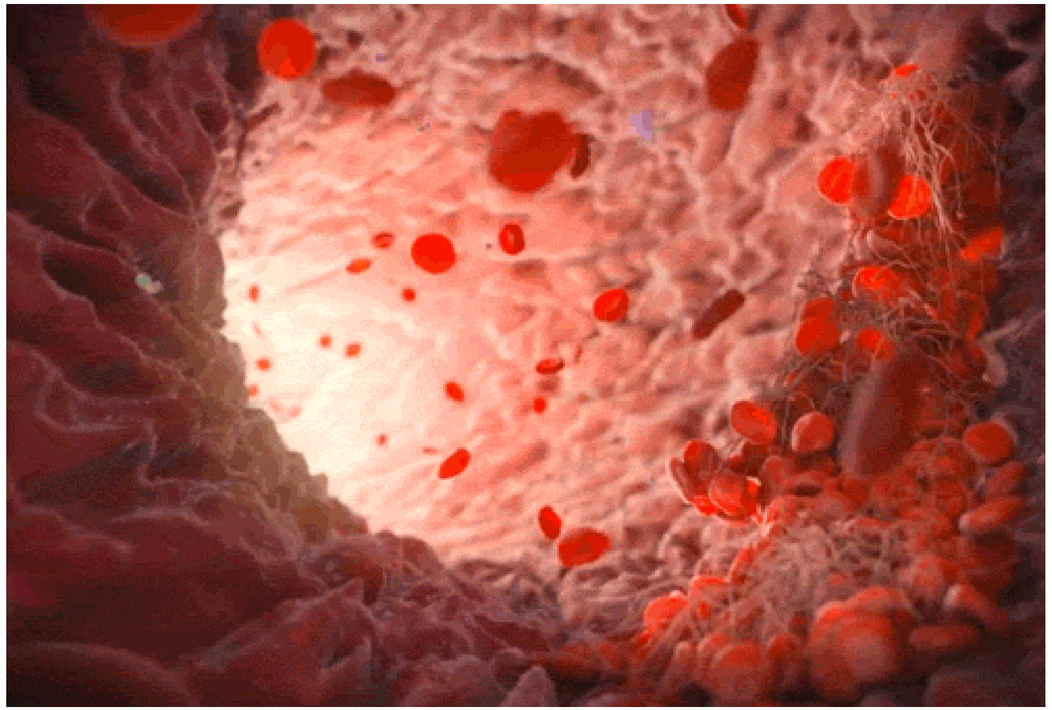
Jordan Schaefer, MD

# STOP-CAT: **S**tandardized **T**hromboprophylaxis for the **O**utpatient **P**revention of **C**ancer **A**ssociated **T**hrombosis



# Disclosures

- Research funding from Pfizer
- Consulting for Pharmacosmos, Novartis



# Two patients

**A. Ms. Smith, age 52**

- Stage IIIC high-grade serous ovarian cancer with peritoneal carcinomatosis
- Starting neoadjuvant carboplatin/paclitaxel

**B. Ms. Johnson, age 55**

- Stage IIIC high-grade serous ovarian cancer with peritoneal carcinomatosis
- Starting neoadjuvant carboplatin/paclitaxel

# Two patients

**A. Ms. Smith, age 52**

- Characteristics:
  - ECOG 1, BMI 31 kg/$m^2$
  - Hemoglobin 11.5 g/dL, plt 420 x $10^9$/L
  - Creatinine clearance normal
  - No bleeding history or active bleeding
  - Family history of venous thromboembolic disease
  - Not on active medications

**B. Ms. Johnson, age 55**

- Characteristics:
  - ECOG 1, BMI 29 kg/$m^2$
  - Hemoglobin 9.4 g/dL, plt 390 x $10^9$/L
  - Creatinine clearance normal
  - Ongoing vaginal bleeding, required transfusion
  - History of gastric ulcer requiring hospitalization 6 months ago
  - History of  seizures, on carbamazepine

# Should you offer thromboprophylaxis?

A) Yes-to both patients with apixaban or rivaroxaban

B) No-neither patient should receive prophylaxis

C) Only patient A should be offered prophylaxis

D) Only patient B should be offered prophylaxis

# Decision

**A. Ms. Smith, age 52**

- Started on apixaban 2.5 mg by mouth every 12 hours after an individualized risk-benefit discussion
  - Reported that her co-pay was acceptable
    - Utilized the co-pay card available from the manufacturer
  - Held anticoagulation before debulking surgery and restarted prophylaxis once hemostasis was achieved

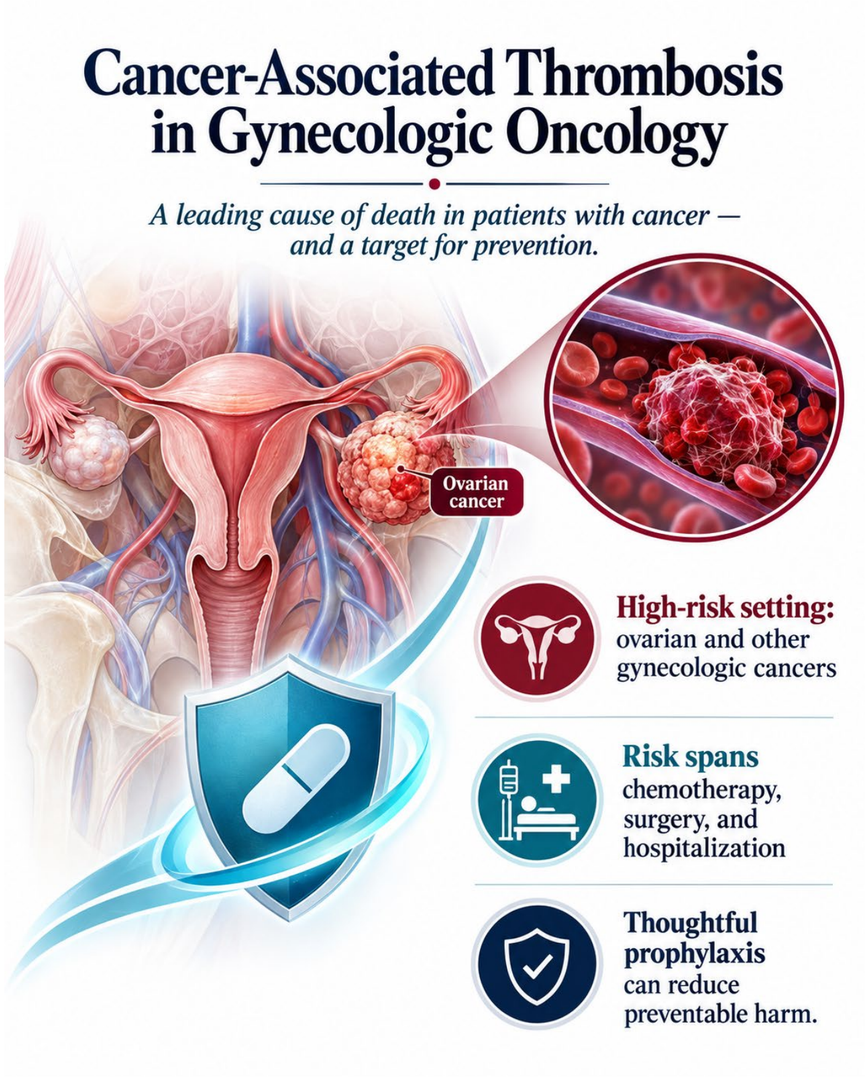
**B. Ms. Johnson, age 55**

- Prophylactic anticoagulation was not offered due to bleeding history and risk factors, drug interaction
  - After surgery, received standard anticoagulation prophylaxis as her bleeding risk factors had improved
    - Mechanical VTE prophylaxis during surgery
  - Was educated on the signs and symptoms of venous thromboembolism as part of the project

- Why do these two patients receive different prophylactic anticoagulation recommendations?

# Cancer Associated Thrombosis: A Leading Cause of Death

- 2nd leading cause of death for patients with cancer
  - One in ten patients
  - Up to one in five depending on risk factors
- >100,000 VTE events per year
- Anticoagulant prophylaxis: NNT 16-35



# Major Primary Thromboprophylaxis Trials in Cancer

## Landmark studies with absolute event rates, NNT, and NNH

### 2009 — PROTECHT

**Population**
Ambulatory solid tumors on chemotherapy

**Intervention vs comparator**
Nadroparin vs placebo

**Efficacy**
VTE: 2.0% vs 3.9%

**Safety**
Major bleeding: 0.7% vs 0%

| ARR | NNT | NNH |
|---|---|---|
| 1.9% | 53 | 143 |

Early LMWH signal

### 2012 — SAVE-ONCO

**Population**
Metastatic or locally advanced solid tumors on chemotherapy

**Intervention vs comparator**
Semuloparin vs placebo

**Efficacy**
VTE: 1.2% vs 3.4%

**Safety**
Major bleeding: 1.2% vs 1.1%

| ARR | NNT | NNH |
|---|---|---|
| 2.2% | 46 | 1000 |

Large LMWH-era trial

### 2019 — AVERT

**Population**
High-risk ambulatory cancer (Khorana ≥2)

**Intervention vs comparator**
Apixaban vs placebo

**Efficacy**
VTE: 4.2% vs 10.2%

**Safety**
Major bleeding: 3.5% vs 1.8%

| ARR | NNT | NNH |
|---|---|---|
| 6.0% | 17 | 59 |

Clear efficacy, bleeding tradeoff

### 2019 — CASSINI

**Population**
High-risk ambulatory cancer (Khorana ≥2)

**Intervention vs comparator**
Rivaroxaban vs placebo

**Efficacy**
180-day VTE: 6.0% vs 8.8%

**Safety**
Major bleeding: 2.0% vs 1.0%

| ARR | NNT | NNH |
|---|---|---|
| 2.8% | 36 | 100 |

Primary endpoint NS at 180 days; intervention-period VTE 2.6% vs 6.4% (NNT 26)

### 2020 — Guntupalli et al.

**Population**
Postoperative gynecologic oncology

**Intervention vs comparator**
Apixaban vs enoxaparin

**Efficacy**
VTE: 1.0% vs 1.5%

**Safety**
Major bleeding: 0.5% vs 0.5%

| ARR | NNT | NNH |
|---|---|---|
| 0.5% | 200 | not applicable |

Similar safety; oral option

NNT/NNH calculated from absolute risk differences using reported point estimates and rounded to the nearest whole number.
NNT = number needed to treat; NNH = number needed to harm; ARR = absolute risk reduction.

PROTECHT 2009; SAVE-ONCO 2012; AVERT 2019; CASSINI 2019; Guntupalli et al. 2020.

# VTE Risk in Ovarian Cancer

- Patients with ovarian cancer have a high risk of cancer associated thrombosis (CAT)
  - 4.7-24% risk depending on the study[1-7]
  - Can result in morbidity and interrupt cancer treatment, including surgery

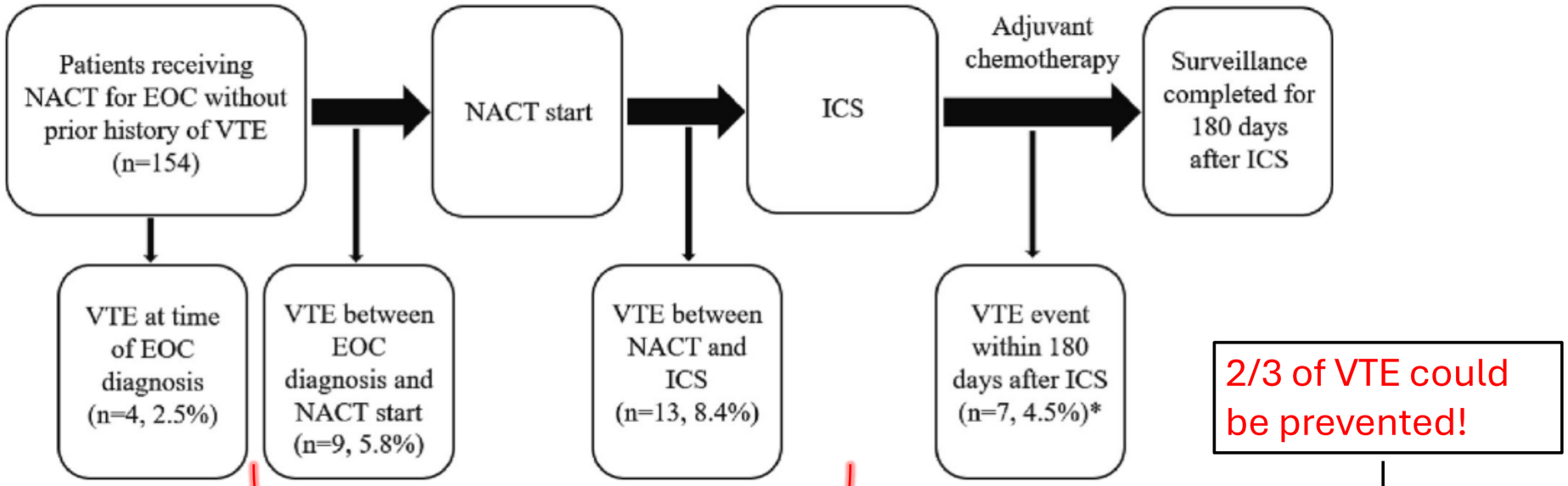



**Fig. 2.** Incidence and timing of venous thromboembolic events Abbreviations: EOC, epithelial ovarian cancer; VTE, venous thromboembolism; NACT, neoadjuvant chemotherapy; ICS, interval cytoreductive surgery.
*Postoperative VTEs occurred between 14 and 64 days after surgery, with 2 occurring prior to 30 day and 5 occurring between 30 and 180 days postoperatively.

# What Do Guidelines Recommend?

| NCCN (2023) | ASCO (2023) | ITAC (2022) | ASH (2021) |
|---|---|---|---|
| • **Consider** anticoagulant prophylaxis for up to 6 months or longer if risk persists | • **May be offered** thromboprophylaxis with apixaban, rivaroxaban, or LMWH provided there are no significant risk factors for bleeding and no drug interactions. | • Prophylaxis with a DOAC is **recommended** for patients receiving systemic anticancer treatment at intermediate to high risk without bleeding risk (Khorana ≥2) | • Suggest thromboprophylaxis with a DOAC (apixaban or rivaroxaban) over no thromboprophylaxis for high-risk patients. No prophylaxis or a DOAC for intermediate risk. |

# Guideline

- 2021 ASH Guidelines[9]
  - Recommend prophylaxis
  - Allow flexibility in risk scoring
    - Validated risk score system
  - Khorana score has not performed well in gyn onc[7]



CLINICAL GUIDELINES

blood advances

Check for updates

American Society of Hematology 2021 guidelines for management of venous thromboembolism: prevention and treatment in patients with cancer

Gary H. Lyman,[1,2,*] Marc Carrier,[3,*] Cihan Ay,[4] Marcello Di Nisio,[5] Lisa K. Hicks,[6] Alok A. Khorana,[7] Andrew D. Leavitt,[8,9] Agnes Y. Y. Lee,[10,11] Fergus Macbeth,[12] Rebecca L. Morgan,[13] Simon Noble,[14] Elizabeth A. Sexton,[15] David Stenehjem,[16] Wojtek Wiercioch,[13] Lara A. Kahale,[17,†] and Pablo Alonso-Coello[18,†]

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**Background:** Venous thromboembolism (VTE) is a common complication among patients with cancer. Patients with cancer and VTE are at a markedly increased risk for morbidity and mortality.

**Objective:** These evidence-based guidelines of the American Society of Hematology (ASH) are intended to support patients, clinicians, and other health care professionals in their decisions about the prevention and treatment of VTE in patients with cancer.

**Methods:** ASH formed a multidisciplinary guideline panel balanced to minimize potential bias from conflicts of interest. The guideline development process was supported by updated or new systematic evidence reviews. The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach was used to assess evidence and make recommendations.

**Results:** Recommendations address mechanical and pharmacological prophylaxis in hospitalized medical patients with cancer, those undergoing a surgical procedure, and ambulatory patients receiving cancer chemotherapy. The recommendations also address the use of anticoagulation for the initial, short-term, and long-term treatment of VTE in patients with cancer.

**Conclusions:** Strong recommendations include not using thromboprophylaxis in ambulatory patients receiving cancer chemotherapy at low risk of VTE and to use low-molecular-weight heparin (LMWH) for initial treatment of VTE in patients with cancer. Conditional recommendations include using thromboprophylaxis in hospitalized medical patients with cancer, LMWH or fondaparinux for surgical patients with cancer, LMWH or direct oral anticoagulants (DOAC) in ambulatory patients with cancer receiving systemic therapy at high risk of VTE and LMWH or DOAC for initial treatment of VTE, DOAC for the short-term treatment of VTE, and LMWH or DOAC for the long-term treatment of VTE in patients with cancer.

Submitted 25 September 2020; accepted 29 October 2020; published online 11 February 2021. DOI 10.1182/bloodadvances.2020003442.

*G.H.L. and M.C. are joint first authors.

†L.A.K. and P.A.-C. are joint last authors.

The full-text version of this article contains a data supplement.

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Lyman GH, et al. American Society of Hematology 2021 guidelines for management of venous thromboembolism: prevention and treatment in patients with cancer. Blood Adv. 2021 Feb 23;5(4):927-974.

## Recommendation 13

For ambulatory patients with cancer at low risk for thrombosis receiving systemic therapy, the ASH guideline panel *recommends* no thromboprophylaxis over parenteral thromboprophylaxis (strong recommendation, moderate certainty in the evidence of effects ⊕⊕⊕◯). For ambulatory patients with cancer at intermediate risk for thrombosis receiving systemic therapy, the ASH guideline panel *suggests* no prophylaxis over parenteral prophylaxis (conditional recommendation, moderate certainty in the evidence of effects ⊕⊕⊕◯). For ambulatory patients with cancer at high risk for thrombosis receiving systemic therapy, the ASH guideline panel *suggests* parenteral thromboprophylaxis (LMWH) over no thromboprophylaxis (conditional recommendation, moderate certainty in the evidence of effects ⊕⊕⊕◯).

**Remarks:** Classification of patients as being low-, intermediate-, or high-risk for VTE should be based on a validated risk-assessment tool (ie, Khorana score) complemented by clinical judgment and experience. The panel noted that, even for patients at high risk for thrombosis, thromboprophylaxis should be used with caution in those with a high risk for bleeding.

## Recommendations 14 and 15

For ambulatory patients with cancer receiving systemic therapy, the ASH guideline panel *recommends* no thromboprophylaxis over oral thromboprophylaxis with VKAs (strong recommendation, very low certainty in the evidence of benefits ⊕◯◯◯ but high certainty about the harms ⊕⊕⊕⊕). For ambulatory patients with cancer at low risk for thrombosis receiving systemic therapy, the ASH guideline panel *suggests* no thromboprophylaxis over oral thromboprophylaxis with a DOAC (apixaban or rivaroxaban) (conditional recommendation, moderate certainty in the evidence of effects ⊕⊕⊕◯). For ambulatory patients with cancer at intermediate risk for thrombosis receiving systemic therapy, the ASH guideline panel *suggests* thromboprophylaxis with a DOAC (apixaban or rivaroxaban) or no thromboprophylaxis (conditional recommendation, moderate certainty in the evidence of effects ⊕⊕⊕◯). For ambulatory patients with cancer at high risk for thrombosis receiving systemic therapy, the ASH guideline panel *suggests* thromboprophylaxis with a DOAC (apixaban or rivaroxaban) over no thromboprophylaxis (conditional recommendation, moderate certainty in the evidence of effects ⊕⊕⊕◯).

**Remarks:** Classification of patients as being at low, intermediate, or high risk for VTE should be based on a validated risk assessment tool (ie, Khorana score) complemented by clinical judgment and experience. The panel noted that, even for patients at high risk for thrombosis, thromboprophylaxis should be used with caution for those at high risk for bleeding. The direct factor Xa inhibitors apixaban and rivaroxaban are the only DOACs that were evaluated for the primary prophylaxis for ambulatory patients with cancer receiving chemotherapy.

# What about gynecologic oncology?

- ERAS Guidelines, Published 2026
- Cite a meta-analysis with 10% rate of VTE during neoadjuvant chemotherapy
- “VTE prophylaxis can be used in the neoadjuvant setting during the course of chemotherapy prior to surgery.”
  - Evidence level: Low
  - Recommendation strength: Weak



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Enhanced recovery after surgery (ERAS®) society guidelines for gynecologic oncology: 2026 update☆

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HIGHLIGHTS

- The third updated review of the ERAS® Society gynecologic oncology guidelines is presented.
- This guideline will help integrate knowledge into practice and align perioperative care globally.
- ERAS teams are encouraged to adopt these recommendations and standardize perioperative pathways where possible.

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ABSTRACT

*Background.* This is the third updated enhanced recovery after surgery (ERAS®) society guideline presenting a consensus for optimal perioperative care in gynecologic oncology surgery.

*Methods.* A database search of publications using Embase and PubMed was performed (2018–2025). Studies for key elements within the ERAS gynecologic oncology protocol were selected with emphasis on meta-analyses, randomized controlled trials, and large prospective cohort studies. These studies were then reviewed and graded according to the grading of recommendations, assessment, development and evaluation (GRADE) system.

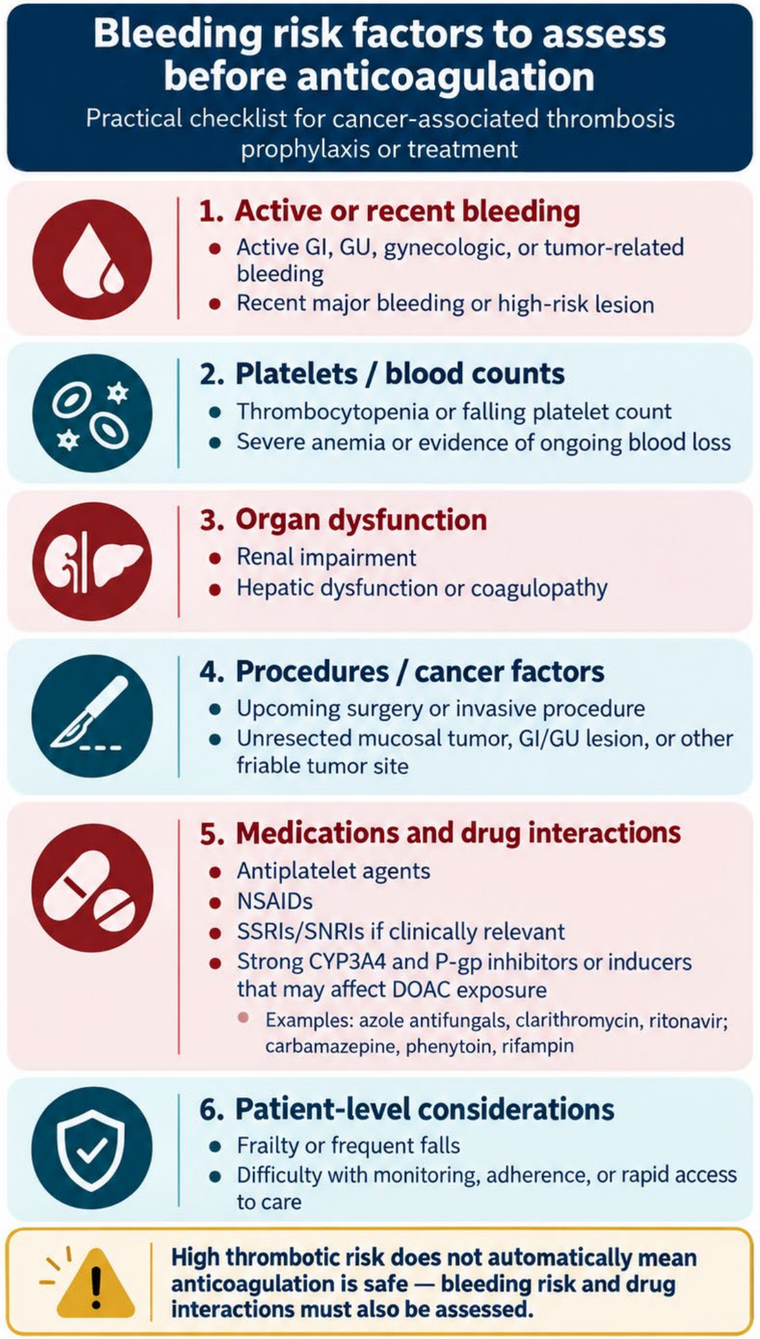
☆ These guidelines were presented in part at the 12th ERAS World Congress in Singapore, on May 14, 2026.

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# Who should not get prophylaxis?

- Cost being a barrier
- Active bleeding
- Bleeding risk factors
  - History
    - Fall risk
  - Labs
    - Organ dysfunction
    - Platelets
  - Drug interactions
    - Antiplatelet drugs
    - NSAIDs
    - DOAC interactions
- Patient preference



# Exclusions (clinical or cost >$30/40 per mo)

## Bleeding risk factors to assess before anticoagulation

Practical checklist for cancer-associated thrombosis prophylaxis or treatment

### Cancer-related factors

- Acute leukemia
- Metastatic brain tumor
- Primary brain tumor
- Expected survival <6 months
- Other as stated by provider in their clinical documentation

### Laboratory / organ function

- Platelets <50 × $10^9$/L
- ALT >5× ULN or bilirubin >2× ULN or cirrhosis
- eGFR <30 mL/min
- Weight <40 kg

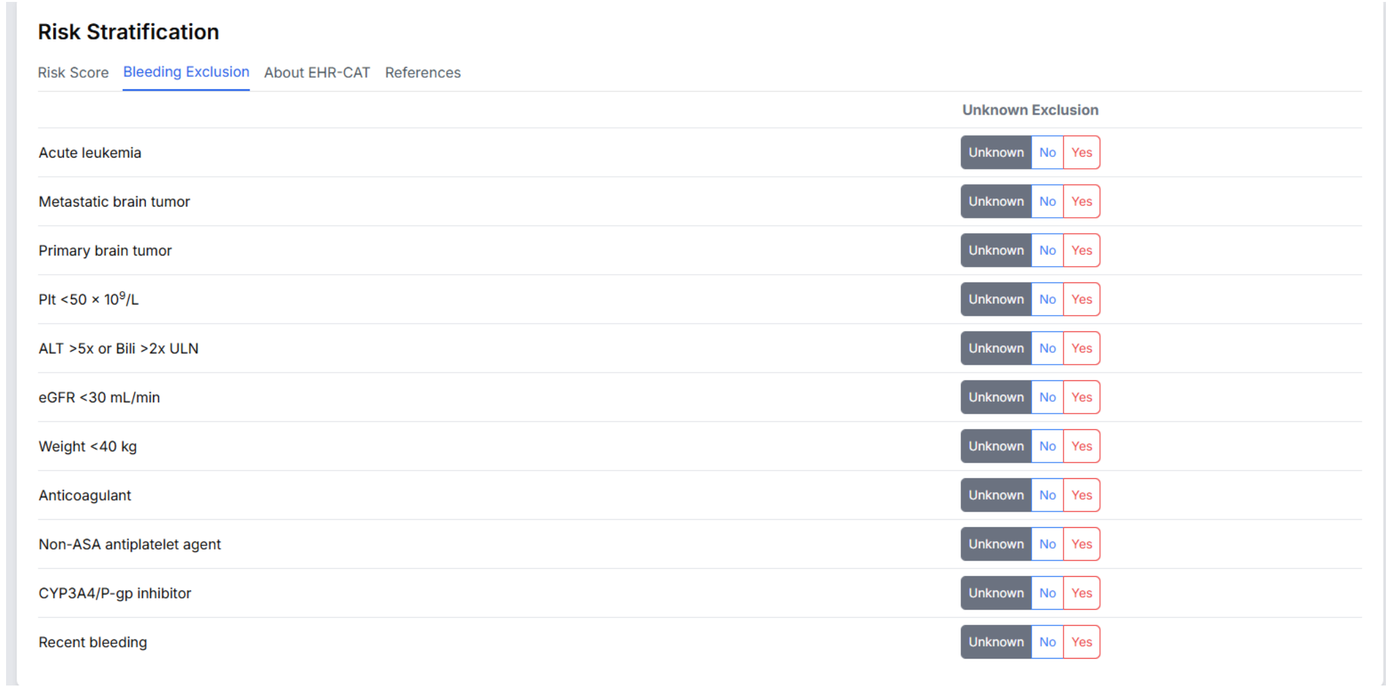
### Medication-related factors

- Anticoagulant
- Non-ASA antiplatelet agent or regular NSAID use
- On a CYP3A4/P-gp inhibitor
  Examples: azole antifungals, clarithromycin, ritonavir

### Clinical history / safety factors

- Recent major bleeding event
  Examples: GI bleeding, heavy vaginal bleeding
- History of gastrointestinal bleeding
- High fall risk
- Uncontrolled hypertension

**High thrombotic risk does not automatically mean anticoagulation is safe — bleeding risk and drug interactions must also be assessed.**



- Drug interactions
  - NSAIDs
  - Aspirin/antiplatelet drugs
  - Antifungals (azoles)
  - ?corticosteroids
  - NK1 antiemetics (fosaprepitant, ariprepitant)
  - Others

| Drug Class | Examples (based on human in vivo data)[1] | Known or Probable Effect | US PI Recommendations |
|---|---|---|---|
| Combined P-gp inhibitor and strong inhibitor of CYP3A4 | cobicistat, conivaptan, indinavir, itraconazole*, ketoconazole**, posaconazole, ritonavir*, saquinavir, telaprevir, telithromycin<br>* cited as example in US PI<br>** cited as example in US PI, with pharmacokinetic data cited | Significant increase in apixaban concentration | Reduce apixaban dose to 2.5mg twice daily.<br>In patients already taking 2.5mg twice daily, avoid coadministration |
| Combined P-gp inhibitor and moderate CYP3A4 inhibitor OR strong CYP3A4 inhibitor alone | clarithromycin*, diltiazem*, dronedarone, erythromycin, fluconazole, mifepristone, nefazodone, verapamil, voriconazole<br>* pharmacokinetic data cited in US PI | Moderate increase in apixaban concentrations in patients with normal renal function.<br>Potentially significant increase in apixaban concentrations in patients with severe renal insufficiency | No dose adjustment recommended |
| Combined P-gp inducer and strong CYP3A4 inducer[3] | carbamazepine*, dexamethasone, rifampin**, St Johns wort*<br>* cited as example in US PI<br>** cited as example in US PI, with pharmacokinetic data cited | Significant reduction in apixaban concentration<br>Effect may persist for several weeks after discontinuation of stong inducers of P-gp and/or CYP3A4 | Avoid use |
| Inducers of P-gp[3] | tipranavir | | Not specifically addressed |
| Strong inducers of CYP3A4[3] | bosentan, efavirenz, etravirine, fosphenytoin, nafcillin, nevirapine, phenobarbital[2], phenytoin*, primidone, rifabutin, rifapentine<br>* cited as example of combined P-gp inducer and strong CYP3A4 inducer in US PI | | Avoid use of phenytoin |

# Traditional risk assessment

- Khorana risk score is the most well studied
- Does not perform well in a gynecologic oncology population

## Khorana Risk Score

Predicts risk of chemotherapy-associated venous thromboembolism (VTE) in ambulatory patients with cancer

| Risk factor | | Criteria | Points |
|---|---|---|---|
|  | **Cancer site (very high risk)** | Stomach, pancreas | **+2** |
|  | **Cancer site (high risk)** | Lung, lymphoma, gynecologic, bladder, testicular | **+1** |
|  | **Platelet count** | ≥350 × $10^9$/L (before chemotherapy) | **+1** |
|  | **Hemoglobin** | <10 g/dL or use of erythropoiesis-stimulating agents | **+1** |
|  | **White blood cell count** | >11 × $10^9$/L (before chemotherapy) | **+1** |
|  | **Body mass index (BMI)** | ≥35 kg/$m^2$ | **+1** |

### Risk categories and estimated VTE risk

| Total score | Risk classification | Original estimated VTE risk* |
|---|---|---|
| **0** | **Low** | 0.8% |
| **1–2** | **Intermediate** | 1.8% |
| **≥3** | **High** | 7.1% |

- Estimated VTE risk is the 2.5-month incidence in the original derivation cohort.
- More recent prophylaxis trials (AVERT, CASSINI) used Khorana ≥2 to identify higher-risk ambulatory cancer patients.
- All patients with ovarian cancer receive +1 point based on cancer site.
- Stage III/IV disease does not independently contribute to the Khorana score.
- A patient with advanced ovarian cancer, normal laboratory values, and BMI <35 may therefore score only 1, despite substantial clinical thrombosis risk.

*Khorana AA, et al. Blood. 2008;111:4902–4907. doi: 10.1182/blood-2007-10-116327*

# Risk Stratification

- EHR-CAT score
  - Improved performance to the Khorana score
  - **Initial publication:** Li A, et al. Derivation and Validation of a Clinical Risk Assessment Model for Cancer-Associated Thrombosis in Two Unique US Health Care Systems. J Clin Oncol. 2023 Jun 1;41(16):2926-2938.
  - **External validation:** Dulberger KN, et al. External validation of a novel cancer-associated venous thromboembolism risk assessment score in a safety-net hospital. Res Pract Thromb Haemost. 2024 Dec 3;9(1):102650.
  - **Validation:** Lanting V, et al. Validation of clinical risk assessment scores for venous thromboembolism in patients with cancer: a population-based cohort study. J Thromb Haemost. 2025 Feb;23(2):600-609.

https://cds.angli-lab.com/en

Table 2.

Patient high-low score groups.

| Risk score | Classification | *n* | Overall VTE incidence at 6 mo, % (*n*) | C statistic (95% CI) | PE/LE-DVT incidence at 6 mo, % (*n*) | C statistic (95% CI) |
|---|---|---|---|---|---|---|
| EHR-CAT (0-5+) | Low risk (2−) | 1271 | 5 (52) | 0.67 (0.63-0.71) | 3.4 (34) | 0.68 (0.63-0.72) |
| | High risk (3+) | 832 | 13.3 (98) | | 10.8 (76) | |
| Khorana score (0-3+) | Low risk (1−) | 1484 | 7.4 (92) | 0.58 (0.54-0.63) | 5.8 (69) | 0.59 (0.54-0.64) |
| | High risk (2+) | 619 | 10.6 (58) | | 7.8 (41) | |

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EHR-CAT, electronic health record cancer-associated thrombosis; LE-DVT, lower extremity deep vein thrombosis; PE, pulmonary embolism; VTE, venous thromboembolism.

Table 2. Performance of EHR-CAT vs Khorana Score for VTE at 6 Months

| Score | Cancer patients, No. (%) (N = 732 594) | Classification | VTE at 6 mo | | | PE or LE-DVT at 6 mo | | |
|---|---|---|---|---|---|---|---|---|
| | | | No. (row %) (n = 34 499) | HR (95% CI) | TD-ROC | No. (row %) (n = 28 341) | HR (95% CI) | TD-ROC |
| EHR-CAT score | | | | | | | | |
| ≤0 | 229 808 (31.4) | Low risk | 3062 (1.3) | 1 [Reference] | 0.70 (0.70-0.70) | 2285 (1.0) | 1 [Reference] | 0.71 (0.71-0.71) |
| 1 | 117 796 (16.1) | | 4059 (3.4) | 2.12 (2.05-2.18) | | 3132 (2.7) | 2.08 (2.01-2.15) | |
| 2 | 116 288 (15.9) | | 5499 (4.7) | 2.99 (2.92-3.11) | | 4350 (3.7) | 3.01 (2.92-3.11) | |
| 3 | 112 900 (15.4) | | 7096 (6.3) | 4.01 (3.90-4.12) | | 5829 (5.2) | 4.12 (3.99-4.25) | |
| 4 | 86 456 (11.8) | High risk | 7102 (8.2) | 5.28 (5.14-5.44) | | 6033 (8.5) | 5.53 (5.36-5.70) | |
| ≥5 | 69 346 (9.5) | | 7681 (11.1) | 7.31 (7.10-7.52) | | 6712 (9.7) | 7.83 (7.59-8.08) | |
| Khorana score | | | | | | | | |
| 0 | 275 609 (37.6) | Low risk | 7447 (2.7) | 1 [Reference] | 0.63 (0.63-0.63) | 5989 (2.2) | 1 [Reference] | 0.63 (0.63-0.63) |
| 1 | 258 259 (35.3) | | 12 019 (4.7) | 1.65 (1.61-1.68) | | 9769 (3.8) | 1.65 (1.61-1.69) | |
| 2 | 139 135 (19.0) | High risk | 9423 (6.8) | 2.45 (2.40-2.51) | | 7829 (5.6) | 2.49 (2.43-2.55) | |
| 3+ | 59 591 (8.1) | | 5610 (9.4) | 3.37 (3.29-3.46) | | 4754 (8.0) | 3.44 (3.35-3.54) | |

Abbreviations: HR, hazard ratio; LE-DVT, lower extremity deep vein thrombosis; TD-ROC, time-dependent receiver operating characteristic; VTE, venous thromboembolism.

# Tool

https://cds.angli-lab.com/en

## Risk Stratification

Risk Score | Bleeding Exclusion | About EHR-CAT | References

| | **Khorana Score: 0** (restricted to 0-3) | **EHR-CAT Score: 0** (restricted to 0-5) |
|---|---|---|
| Cancer site/histology | Unknown 0<br>Other 0<br>Lung, kidney, bladder, testicular, ovarian, uterine, aggresive lymphoma, cervical +1<br>Pancreas, stomach +2 | Unknown 0<br>Other 0<br>Colorectal +1<br>Lung, kidney, bladder, testicular, ovarian, uterine, aggresive lymphoma, sarcoma, brain, myeloma, acute lymphocytic leukemia +2<br>Pancreas, stomach, esophageal, biliary, gallbladder +3 |
| Pretherapy BMI ≥35 kg/m$^2$ | Unknown 0 \| No 0 \| Yes +1 | Unknown 0 \| No 0 \| Yes +1 |
| Pretherapy WBC >11 × 10$^9$/L | Unknown 0 \| No 0 \| Yes +1 | Unknown 0 \| No 0 \| Yes +1 |
| Pretherapy Hgb <10 g/dL | Unknown 0 \| No 0 \| Yes +1 | Unknown 0 \| No 0 \| Yes +1 |
| Pretherapy Plt ≥350 × 10$^9$/L | Unknown 0 \| No 0 \| Yes +1 | Unknown 0 \| No 0 \| Yes +1 |
| Advanced cancer stage (III-IV) | | Unknown 0 \| No 0 \| Yes +1 |

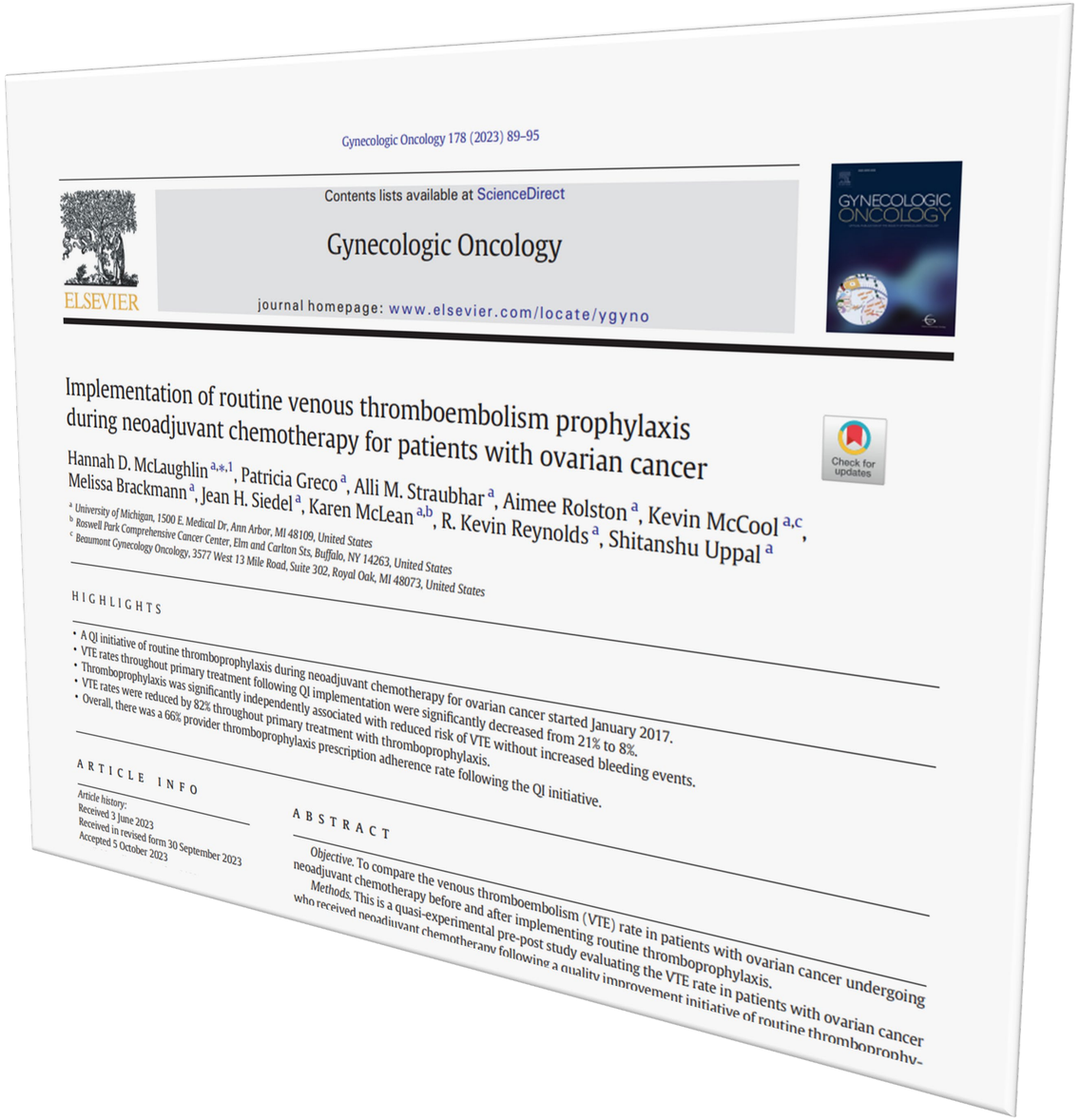
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# Risk Stratification Simplified

- +2 for ovarian cancer
- +1 for advanced stage
- [-1 for East/South Asian or Pacific Islander]
  - VTE risk 6%
    - +BMI/WBC/anemia/thrombocytosis/history of VTE/immobility/hospitalizations
      - Risk 9% with one additional risk factor
      - Risk 11%+ with two or more additional risk factors
  - **All advanced stage ovarian cancer are high risk without additional risk stratification other than East/South Asian/Pacific Islander**

# Michigan Medicine Experience

- Ovarian cancer
  - Khorana score performs poorly
- Routine thromboprophylaxis January 2017
- Pre-intervention: 3.7% prophylaxis
- Post-intervention: 65% prophylaxis
  - Improved provider uptake over time



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Implementation of routine venous thromboembolism prophylaxis during neoadjuvant chemotherapy for patients with ovarian cancer

Hannah D. McLaughlin [a,*,1], Patricia Greco [a], Alli M. Straubhar [a], Aimee Rolston [a], Kevin McCool [a,c], Melissa Brackmann [a], Jean H. Siedel [a], Karen McLean [a,b], R. Kevin Reynolds [a], Shitanshu Uppal [a]

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HIGHLIGHTS

- A QI initiative of routine thromboprophylaxis during neoadjuvant chemotherapy for ovarian cancer started January 2017.
- VTE rates throughout primary treatment following QI implementation were significantly decreased from 21% to 8%.
- Thromboprophylaxis was significantly independently associated with reduced risk of VTE without increased bleeding events.
- VTE rates were reduced by 82% throughout primary treatment with thromboprophylaxis.
- Overall, there was a 66% provider thromboprophylaxis prescription adherence rate following the QI initiative.

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ABSTRACT

*Objective.* To compare the venous thromboembolism (VTE) rate in patients with ovarian cancer undergoing neoadjuvant chemotherapy before and after implementing routine thromboprophylaxis.
*Methods.* This is a quasi-experimental pre-post study evaluating the VTE rate in patients with ovarian cancer who received neoadjuvant chemotherapy following a quality improvement initiative of routine thromboprophy-

# Inclusion/exclusion

- Adults
- Stage III or IV ovarian, fallopian tube, or primary peritoneal cancer
- 2009-2014 pre-intervention
  - 2015-2016 excluded due to variable prophylaxis patterns
- 2017-2021 post-intervention



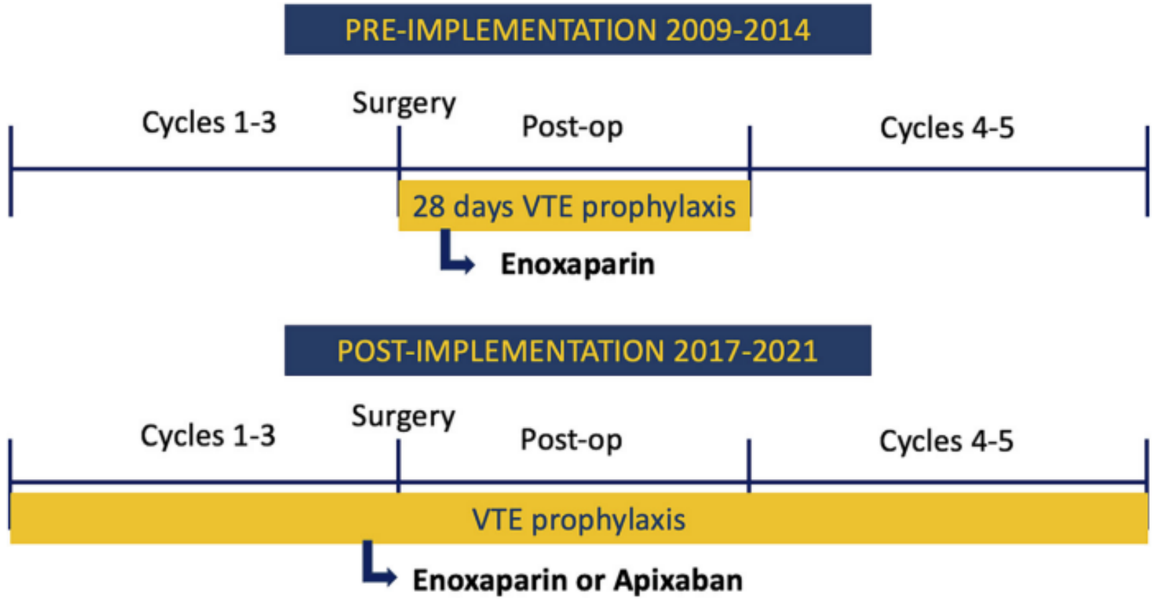
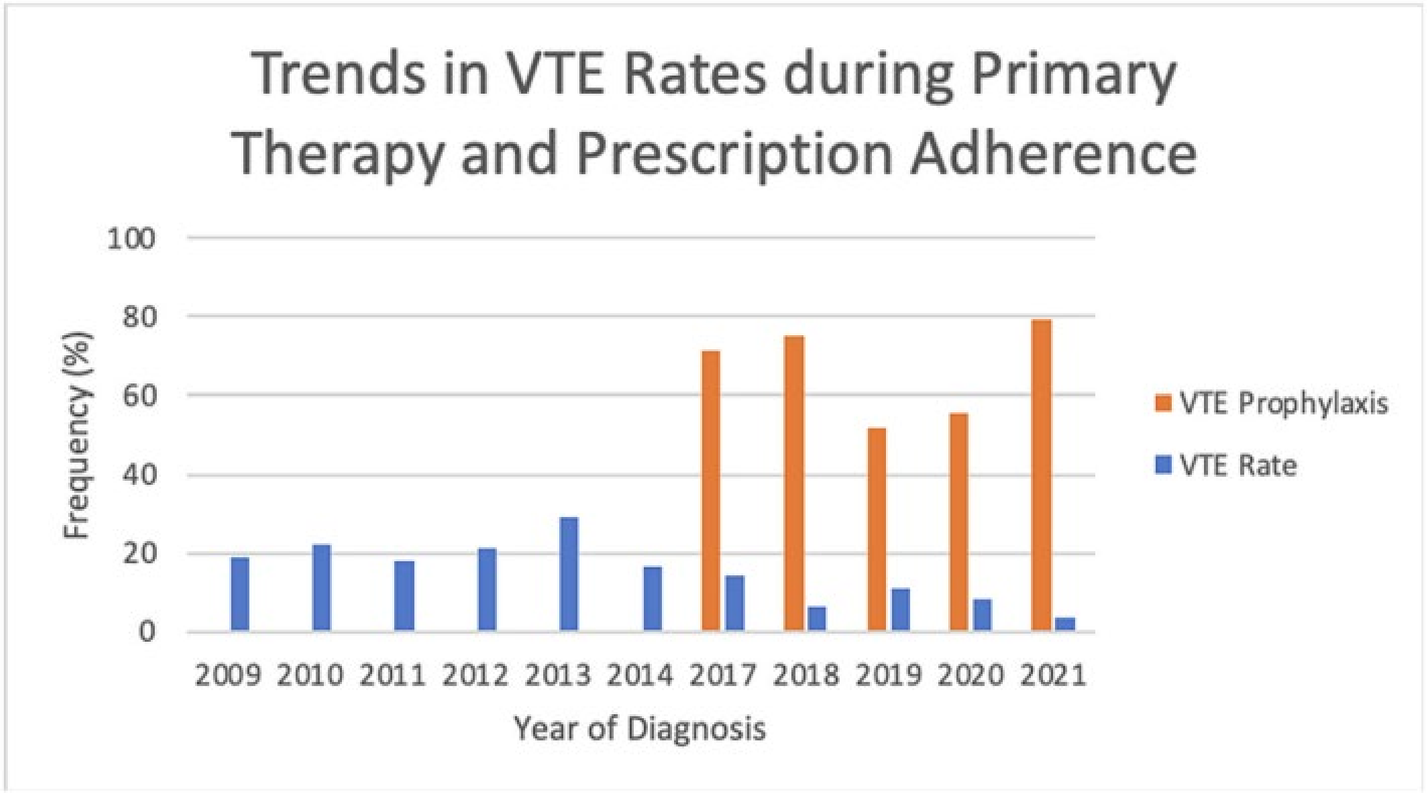



**Fig. 1.** Timeline displaying the standard thromboprophylaxis for patients in the pre-implementation and post-implementation timeframes.

# Prophylaxis



# Michigan Medicine Experience

- Pre-intervention had 21.3% rate of VTE
- Post-intervention 8.4% rate of VTE
- No difference in major bleeding (0.0% versus 0.68%)
- Multivariate analysis showed only prophylaxis to be associated with reduced VTE

# Results

**Table 2**
Comparison of VTE, bleeding, and transfusion events in the Intention-to-Treat Analysis and the Per-Treatment Analysis.

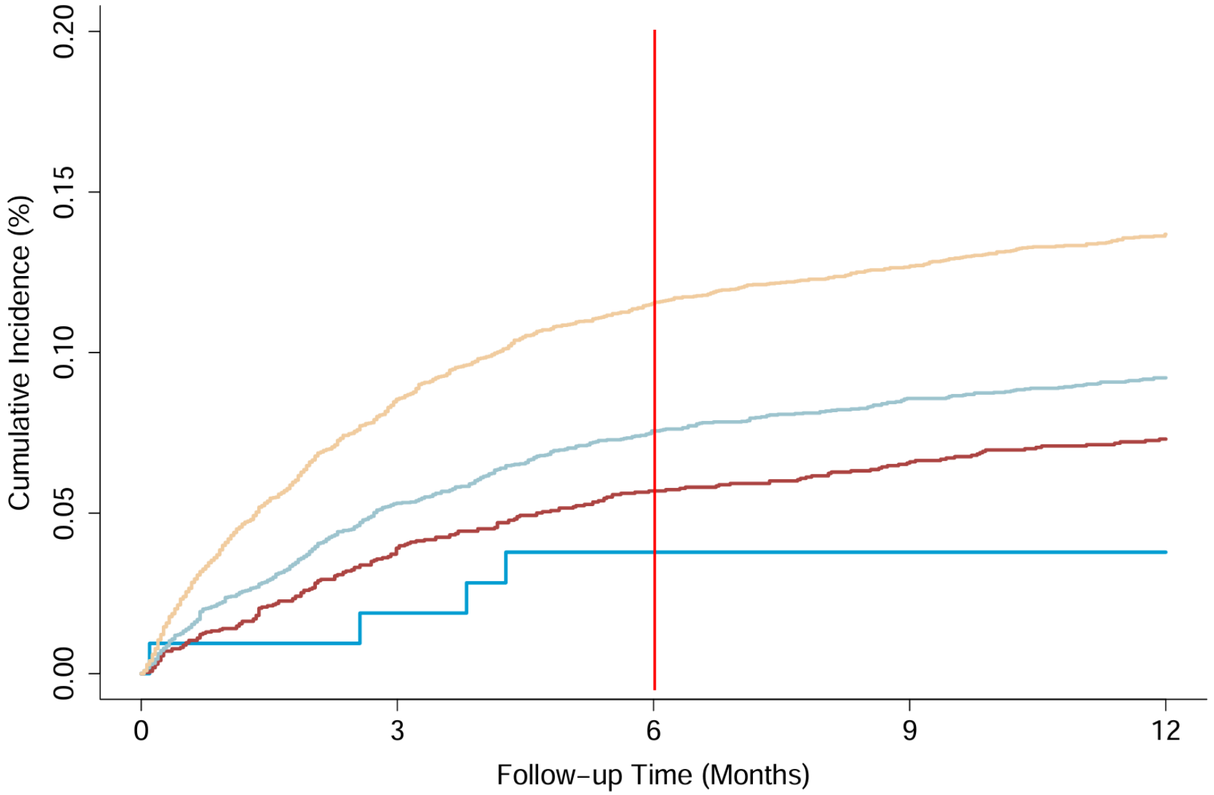
| Characteristics | Intention-to-treat (Pre-Post) Analysis | | | Per-treatment group (Efficacy) Analysis | | |
|---|---|---|---|---|---|---|
| | Pre-Implementation | Post-Implementation | | No VTE Prophylaxis with NACT | VTE Prophylaxis with NACT | |
| | $n = 136$ | $n = 154$ | p-value | $n = 184$ | $n = 106$ | p-value |
| Total VTE Events[a] | 29 (21.32) | 13 (8.44) | **0.002** | 37 (20.11) | 5 (4.72) | **<0.01** |
| NACT VTE | 14 (10.29) | 10 (6.49) | 0.241 | 21 (11.41) | 3 (2.83) | **0.013** |
| Post-operative VTE[b] | 6 (4.41) | 2 (1.30) | 0.106 | 7 (3.80) | 1 (0.94) | 0.265 |
| Adjuvant Chemotherapy VTE | 11 (8.09) | 1 (0.65) | **0.002** | 11 (5.98) | 1 (0.94) | 0.062 |
| Bleeding events during NACT | 0 (0) | 1 (0.68) | 0.63 | 1 (1.32) | 0 (0) | 0.239 |
| Total Transfusion Events | 61 (53.04) | 53 (35.81) | **0.005** | 68 (43.31) | 46 (43.40) | 0.989 |
| NACT Transfusion | 25 (18.38) | 11 (7.14) | **0.004** | 28 (15.22) | 8 (7.55) | 0.056 |
| Intraoperative Transfusion | 6 (4.41) | 12 (7.79) | 0.234 | 9 (4.89) | 9 (8.49) | 0.221 |
| Post-operative Transfusion | 29 (21.32) | 26 (16.88) | 0.336 | 33 (17.93) | 22 (20.75) | 0.555 |
| Adjuvant Chemotherapy Transfusion | 31 (22.79) | 22 (14.29) | 0.061 | 35 (19.02) | 18 (16.98) | 0.665 |

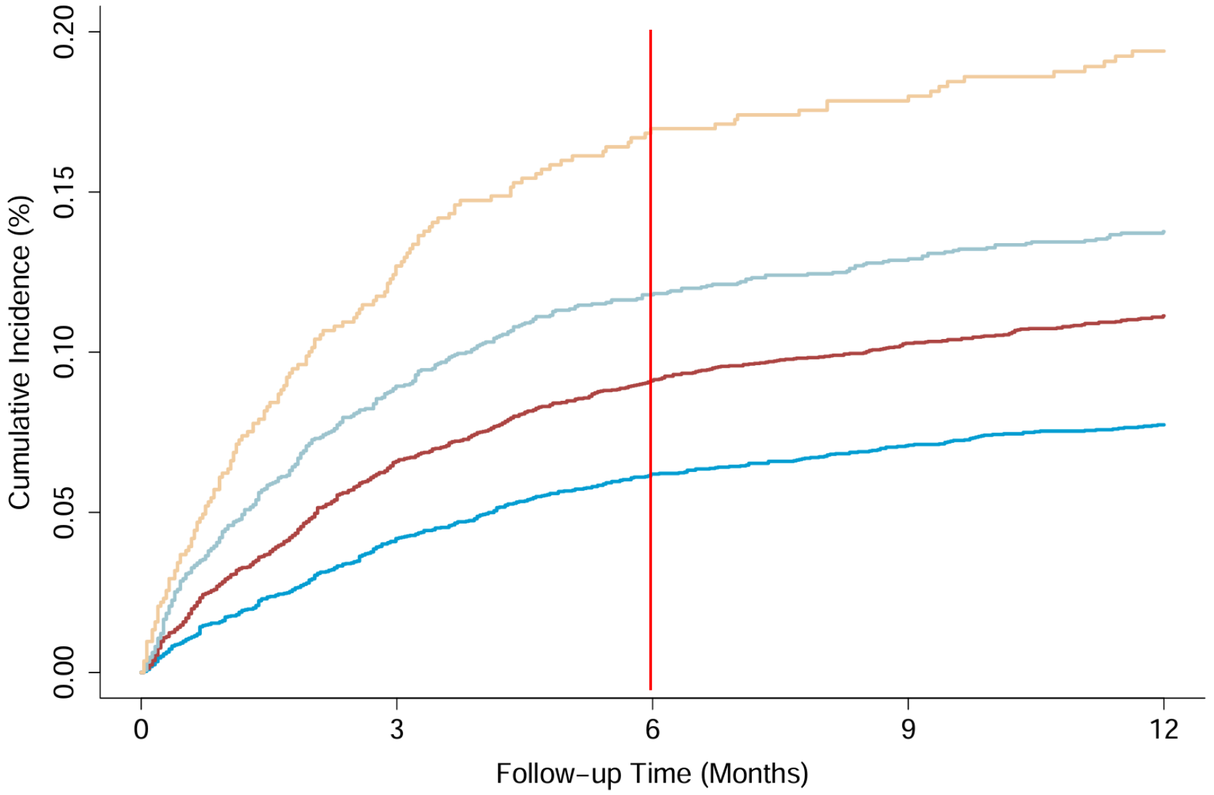
Data are n (%) unless otherwise specified.
[a] Exclude VTE upon presentation or during surveillance.
[b] Within 30 days of surgery.

# Performance of EHR-CAT vs KS in ovarian cancer patients (preliminary data)

**EHR-CAT 5**: 11.5% (n=6702)
**EHR-CAT 4**: 7.6% (n=5292)
**EHR-CAT 3**: 5.7% (n=2701)
**EHR-CAT 2**: 3.8% (n=106)

**KS 4**: 17.0% (n=828)
**KS 3**: 11.8% (n=2728)
**KS 2**: 9.1% (n=5910)
**KS 1**: 6.2% (n=5335)




EHR-CAT by definition should have a minimum score of 3 (unless Asian race)
Khorana score misclassifies patients as low-risk when they are high-risk

# Work of Others

- Based on use of Khorana/Protect score, 59% received prophylaxis
  - 3.2% VTE at 6 months versus 7.7%
  - 16.8% deaths with thromboprophylaxis versus 31.3% without
    - Improved outcomes, association with reduced mortality

## Impact of Venous Thrombosis Prevention in Ambulatory Oncology: Importance of Guideline Adherence

Chris E. Holmes, MD, PhD[1,2,3]; Karlyn A. Martin, MD, MS[1,2,3]; Derek Devine, MS[4]; Jacob Barker, PharmD[3]; Peter W. Callas, PhD[4,5]; Karen Libby, RN[3]; Emily Parenteau, APRN[3]; Mary Cushman, MD, MSc[1,2]; and Steven Ades, MD, MSc[1,2,3]

DOI https://doi.org/10.1200/OP-25-01211

**ABSTRACT**

**PURPOSE** Despite strong evidence and guidelines supporting prophylactic anticoagulation for ambulatory patients with cancer starting systemic cancer-directed therapy who are at high risk of venous thromboembolism (VTE), uptake in practice is limited. We evaluated the real-world impact of prophylactic anticoagulation in such patients receiving guideline-based care.

**METHODS** We conducted an observational cohort study of patients assessed as part of a multidisciplinary VTE prevention program (the Vermont model) from 2016 to 2021. For this study, we included outpatients at high risk of VTE based on a Khorana risk score or Protecht risk score of ≥3. Based on the individualized decision making, patients either received or did not receive prophylactic anticoagulation. The primary outcome was VTE at 6 months after risk assessment. The secondary outcome was all-cause mortality at 6 months.

**RESULTS** Of 573 high-risk patients assessed during the study period, 340 (59%) received thromboprophylaxis and 233 (41%) did not. Eleven (3.2%) on thromboprophylaxis developed a VTE within 6 months, compared with 18 (7.7%) not on thromboprophylaxis. After adjusting for age, sex, BMI, cancer stage, chemotherapy, immunotherapy, distance from center, and history of VTE, thromboprophylaxis reduced VTE (adjusted odds ratio [OR], 0.36 [95% CI, 0.16 to 0.80]) compared with no thromboprophylaxis. Of deaths within 6 months, 57 (16.8%) occurred in the thromboprophylaxis group versus 73 (31.3%) in the no thromboprophylaxis group (adjusted OR, 0.46 [95% CI, 0.30 to 0.71]).

**CONCLUSION** Ambulatory patients with cancer at high risk of VTE who received prophylactic anticoagulation had improved clinical outcomes with fewer VTE events and less mortality. Our real-world data support available clinical trial data and underscore the importance of the provision of guideline-directed care in the cancer outpatient setting.

**ACCOMPANYING CONTENT**

Appendix

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# Two patients

## A. Ms. Smith, age 52

Baseline Risk



VTE (at 6 month) 9%



MB (at 6 month) 1%



CRNMB (at 6 month) 3.2%

## B. Ms. Johnson, age 55



With Low-dose DOAC (apixaban or rivaroxaban)





VTE (intention-to-treat) 5.04%





VTE (on-treatment) 2.70%





MB (on-treatment) 1.96%





CRNMB (on-treatment) 4.1%

MB: Major Bleeding CRNMB: Clinically Relevant Non-Major Bleeding
intention-to-treat: risk with usual use of the medication, including interruption, non-adherence, and early discontinuation
on-treatment: risk while actively receiving the medication

# MOQC Measure

- ~60% rate of high-risk patients received prophylaxis through a similar but more resource intensive intervention
  - Khorana or Protecht score ≥3[10]
- Other intervention increased education rate to 100% and risk assessment to 98%[11]
- MOQC: Could consider 30% initial goal



# Gynecologic Oncology Thromboprophylaxis Intervention

## An EHR-CAT-guided prophylaxis approach for ambulatory gynecologic oncology patients

**1** Ambulatory gynecologic oncology patient starting systemic therapy



**2** Bleeding + medication interaction safety review

- Bleeding risk
- Medication interactions
- Patient-specific factors

**3** Shared decision-making



**4** Appropriate action

- Offer thromboprophylaxis
- Defer if unsafe + reassess

## Why this matters

- Reduce preventable VTE
- Improve patient safety
- Standardize appropriate prophylaxis decisions
- Support quality improvement



## Right patient. Right time. Right prophylaxis decision.

Prediction + safety assessment + workflow integration = better care.

**Footnote:** In ambulatory gynecologic oncology, many patients are already clinically high risk; EHR-CAT may still support risk stratification but is not required as a separate workflow step.

# Take home messages

- Patients with advanced ovarian cancer are at high risk for VTE
- Guidelines support offering prophylaxis to risk-stratified patients
  - Need to consider bleeding risk, drug interactions, and preferences
  - Weak recommendation
- MOQC plans to implement a multicenter ambulatory prophylaxis intervention
  - Implementation materials available to support the intervention

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**Design: systematic review, Result: 12.3% of patients with VTE undergoing NACT, conclusion "VTE prophylaxis may be considered in patients with ovarian cancer undergoing NACT."**

2. McLaughlin HD, Greco P, Straubhar AM, et al. Implementation of routine venous thromboembolism prophylaxis during neoadjuvant chemotherapy for patients with ovarian cancer. Gynecol Oncol. Nov 2023;178:89-95. doi:10.1016/j.ygyno.2023.10.001

**Design: pre-post intervention review, Result: 21.3% pre-intervention rate of VTE declined to 8.4% post-intervention**

3. Strom Kahr H, Christiansen OB, Juul Riddersholm S, et al. The timing of venous thromboembolism in ovarian cancer patients: A nationwide Danish cohort study. J Thromb Haemost. Apr 2021;19(4):992-1000. doi:10.1111/jth.15235

**Design: Danish Gynecologic Cancer Database, 2005-2014, Result: 7.2% 2-year cumulative incidence of VTE after ovarian cancer diagnosis, highest in the first year. Risk factors: Past VTE, chemotherapy or VEGF inhibitors, clear cell histopathology, and stage III/IV.**

4. Takahashi Y, Fujiwara H, Yamamoto K, et al. Incidence and risk factors for venous thromboembolism in gynecological cancer: the GOTIC-VTE trial. J Thromb Thrombolysis. Feb 2025;58(2):299-308. doi:10.1007/s11239-024-03055-1

**Design: Prospective cohort study in Japan, 13.7% VTE at baseline (2.1% symptomatic). 4.7% composite rate of VTE over the next year (symptomatic and incidental requiring treatment). Chemotherapy was a risk factor for VTE at 1 year.**

5. Penfound S, Lukey A, Hodgson J, Hopman WM, Hanley GE, Othman M. Incidence and risk factors of venous and arterial thromboembolic events among patients with ovarian cancer- data from a large Canadian database. Gynecol Oncol. Jun 2024;185:116-120. doi:10.1016/j.ygyno.2024.02.011

**Design: Retrospective cohort study of a cancer registry, 1996-2017. 9.4% VTE incidence. Sepsis associated with thrombosis.**

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**Design: Retrospective cohort study of patients with advanced stage ovarian cancer. 21.4% incidence of VTE. Khorana score not associated with risk. Two-thirds may have been prevented. These data support consideration of thromboprophylaxis in all patients with advanced stage EOC undergoing NACT.**

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**Design: Retrospecive cohort study of patients wityh ovarian cancer. 24% incidence of VTE; 32% during NACT. Khorana score did not correlate.**

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10. Holmes, C., Karlyn A. Martin, S. Ades, et al. "Impact of Venous Thrombosis Prevention in Ambulatory Oncology: Importance of Guideline Adherence." JCO Oncology Practice, 2026, doi:10.1200/OP-25-01211.

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# Questions?

## Discussion and audience Q&A



Thank you for your attention