DVT Prophylaxis In Pregnancy: What Should We Do?

Amy Sullivan, MD
Maternal-Fetal Medicine
University of Utah School of Medicine

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DVT prophylaxis

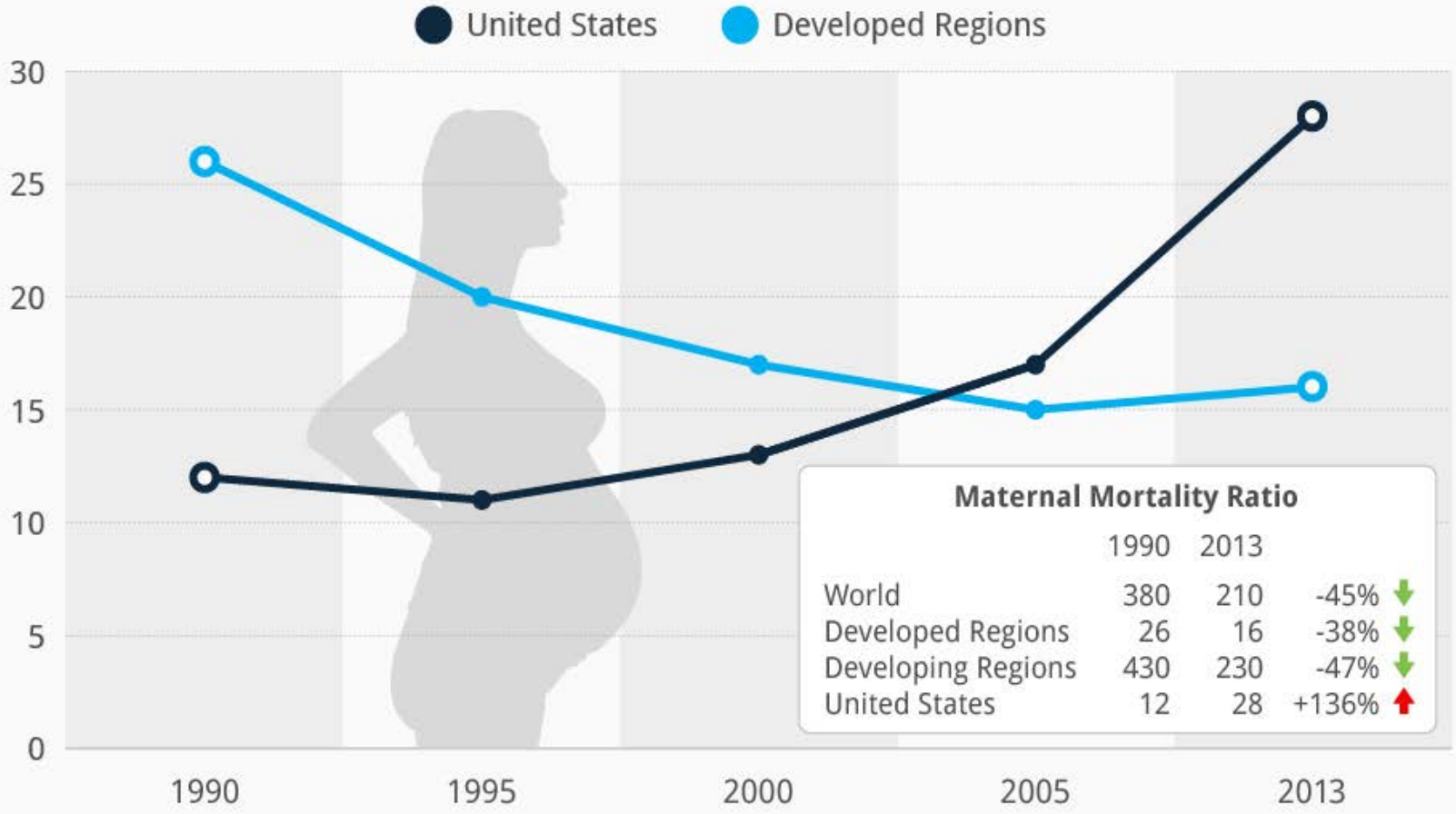
- **Cesarean section**
  - Most controversial
  - Limited data
  - Practice varies widely

Objectives

- Review rationale for DVT prophylaxis
- Discuss risk factors for DVT
- Present current controversies
- Make recommendations for prophylaxis

Maternal Deaths in the U.S. Are on the Rise

Maternal mortality ratio (number of maternal deaths per 100,000 live births)



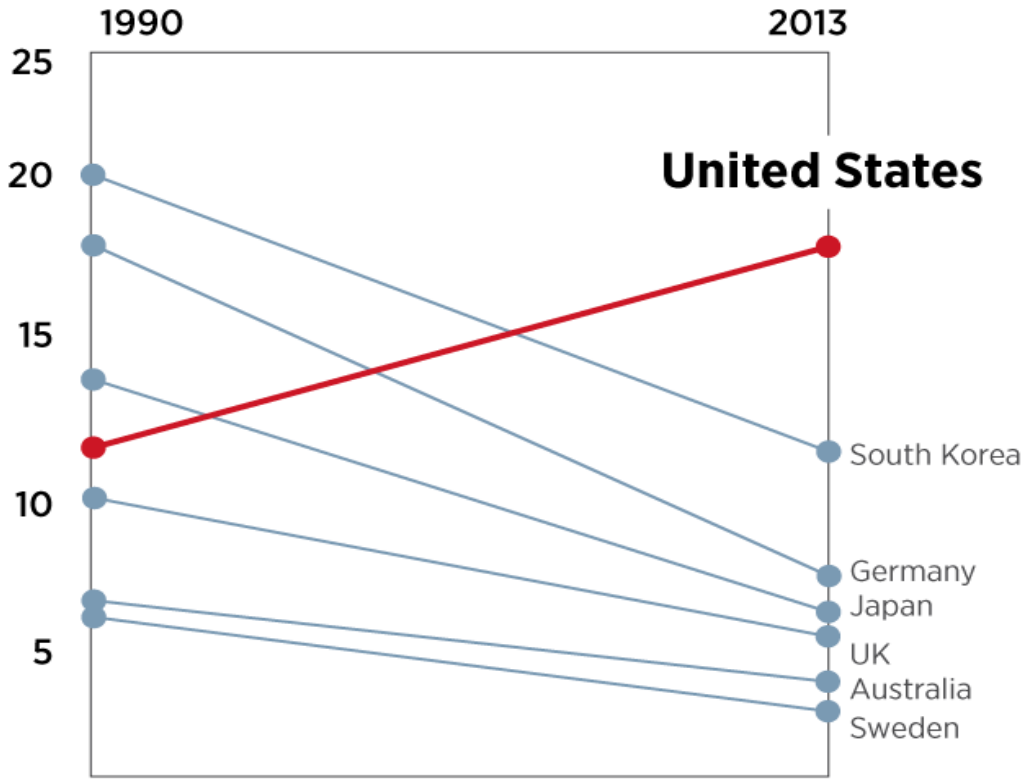
Maternal Mortality Ratio

	1990	2013	
World	380	210	-45% ↓
Developed Regions	26	16	-38% ↓
Developing Regions	430	230	-47% ↓
United States	12	28	+136% ↑

Source: World Health Organization

Mashable statista

Pregnancy-related deaths per 100,000 live births



Source: Institute for Health Metrics and Evaluation
Credit: Sarah Frostenson, Vox

WSWS.ORG

The New York Times

Maternal Mortality Rate in U.S. Rises, Defying Global Trend, Study Finds

Sabrina Tavernise Septmber 21, 2016

If Americans Love Moms, Why Do We Let Them Die?

Nicholas Kristof July 29, 2017

Fox News Health

US maternal mortality rate is twice that of Canada, says UN

November 12, 2015

WSJ

More Pregnant Women Are Dying in Rural America: Why?

Amber Krosel October 2, 2017

CNN

Giving Birth in America is More Dangerous Than You Think

Kelly Wallace April 2017

NPR Special series: Lost mothers

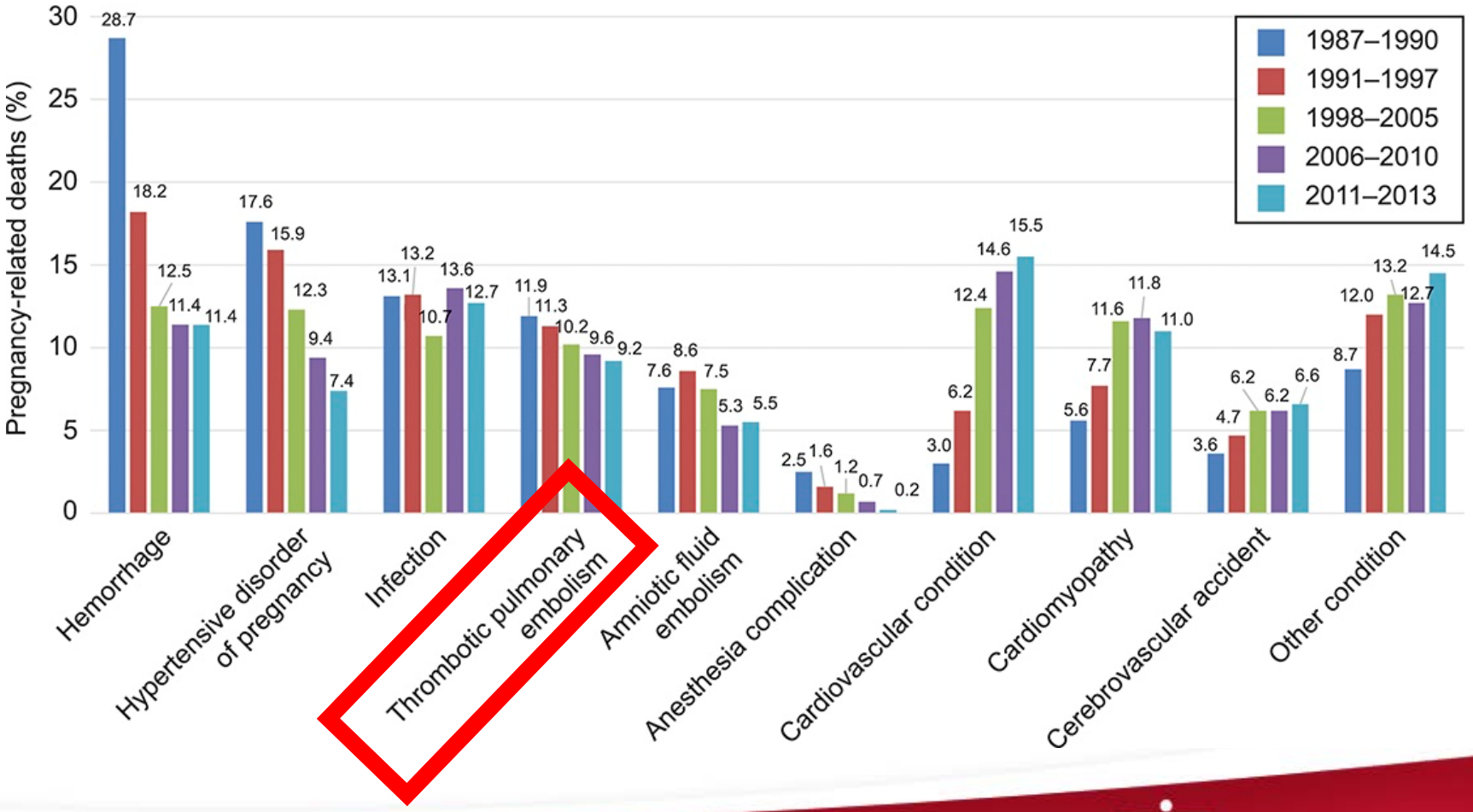
U.S. Has The Worst Rate Of Maternal Deaths In The Developed World

Nina Martin May 12, 2017

US Pregnancy Related Mortality

- CDC data:
  - **700-900** maternal deaths/year
- Estimates by WHO, UNICEF, UNFPA, The World Bank, United Nations Population Division:
  - **1,200** maternal deaths/year
  - **60,000** “near fatal” events/year
- Reported that 50% deaths are preventable

Pregnancy Related Mortality: 1987-2010



Creanga, **Obstet Gynecol** 2017

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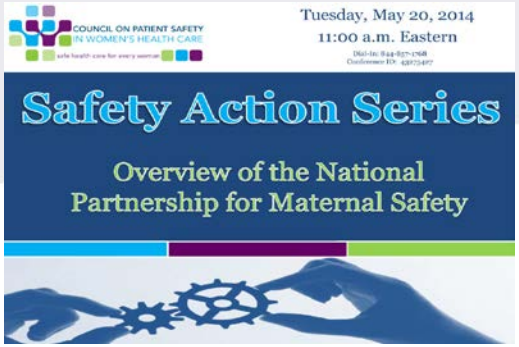

AWHONN
PROMOTING THE HEALTH OF WOMEN AND NEWBORNS

ALLIANCE FOR INNOVATION ON MATERNAL HEALTH AIM

CMQCC
California Maternal Quality Care Collaborative

ACOG
THE AMERICAN CONGRESS OF OBSTETRICIANS AND GYNECOLOGISTS

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DVT Prophylaxis

- 2008: DVT quality measures
  - Joint Commission on Patient Safety
  - National Quality Forum
- 2017: DVT measures available to meet hospital accreditation requirements

Thromboembolism in pregnancy

- 4-5 x fold increased risk vs non-pregnant
- Approximately 1/1000 pregnant women
- 10% of maternal deaths in the United States
- C/S: 2-5x the risk vs. NSVD

Normal physiology

- Anti-coagulant factors decrease:
  - Protein S
  - Anti-thrombin
- Pro-coagulant factors increase:
  - factors II, VII, VIII, X, XII, XIII
  - fibrinogen
- Pro-hemostatic factor von Willebrand factor increases
- Fibrinolytic inhibitor activity increases:
  - PAI-1 and PAI-2

Risk Factors for DVT

- Pregnancy
- Surgery

Obesity
Medical co-morbidities
Thrombophilias
Prior thrombosis
Smoking
Hemorrhage
Infection
AMA

DVT Prophylaxis for C/S

Pneumatic Compression

VS

Pharmacologic treatment

Mechanical Prophylaxis

- Decision Analysis 2006:
  - Mechanical compression was a safe and cost effective strategy

- ACOG *Practice Bulletin #12,* 2011:
  - based on extrapolation from perioperative data, placement of pneumatic compression devices before cesarean delivery is recommended for all women not already receiving thromboprophylaxis.

Casale, **Obstet Gynecol** 2006

Thromboprophylaxis after Cesarean Delivery: A Decision Analysis

- Heparin prophylaxis reduced the risk of DVT; pneumatic compression had the lowest number of adverse events.
- Limitations: “Some data were obtained from studies that included older, non-pregnant patients who underwent gynecologic, general surgery, or orthopedic procedures.”

Quinones, **Obstet Gynecol** 2005

Preventing deep vein clots in pregnancy and after the birth

Cochrane Review February 2014

16 trials, 2592 women:

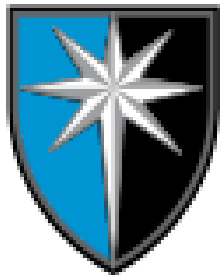
"We found no evidence to suggest that using heparin in pregnancy or after a caesarean birth reduces the risk of maternal death, DVT or PE."

Preventing deep vein clots in pregnancy and after the birth

Cochrane Review February 2014

"There is insufficient evidence on which to base recommendations for thromboprophylaxis during pregnancy and the early postnatal period, with the small number of differences detected in this review being largely derived from trials that were not of high methodological quality."

Pharmacologic



Royal College of Obstetricians & Gynaecologists

- Pioneered efforts to decrease maternal mortality
- 1995: Developed guidelines for DVT prophylaxis using heparin.
- Most comprehensive inclusion criteria

Royal College of Obstetricians & Gynaecologists

- Maternal deaths from PE
  - Pre-guideline: 1.56/100,000 live births (33 deaths)
  - Post guideline: 0.7/100,000 live births (16 deaths)
- Adherence
  - Pre: 5.7% received ppx
  - Post: 96.1% received ppx

RCOG press 2015 Guimicheva, **Br J Haematol** 2015

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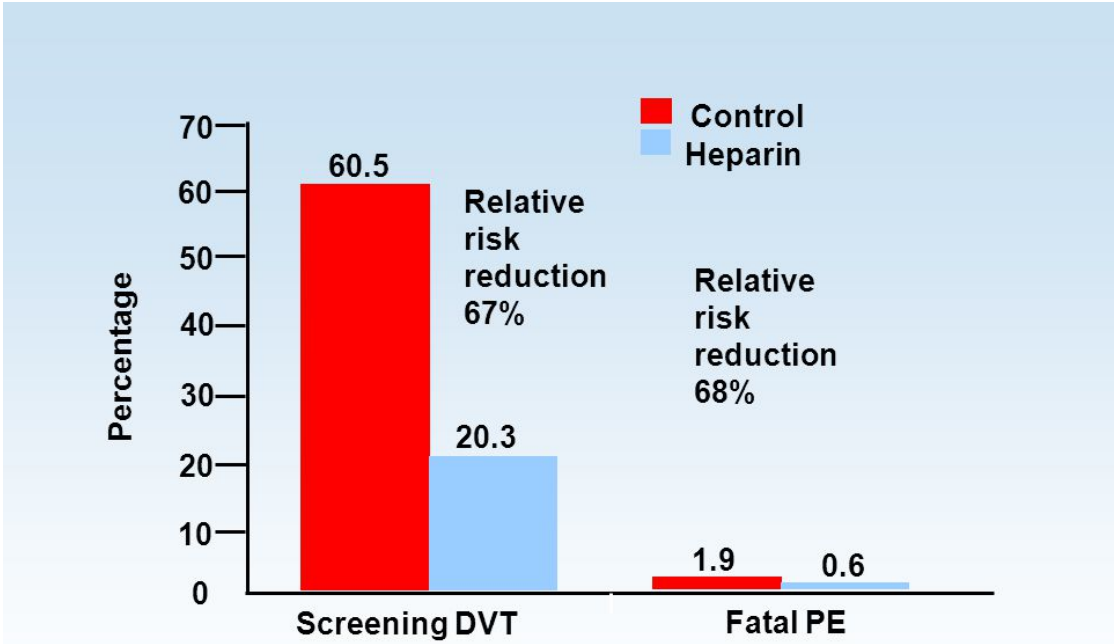
Reduction in Fatal Pulmonary Embolism and Venous Thrombosis by Perioperative Administration of Subcutaneous Heparin



Collins. N Engl J Med. 1988;318:1162-1173.

Collins, NEJM 1988

Reduction in Fatal Pulmonary Embolism and Venous Thrombosis by Perioperative Administration of Subcutaneous Heparin

Table 4. Pulmonary Embolism and Deaths Reported in All Randomized Controlled Trials of Prophylactic Subcutaneous Heparin in General, Orthopedic, and Urologic Surgery.

	Nonfatal Pulmonary Embolism		Fatal Pulmonary Embolism		Fatal Hemorrhage		Other or Unknown Causes of Death	
	Heparin	Control	Heparin	Control	Heparin	Control	Heparin	Control
International Multicentre Trial	14/2230	19/2250	6/2230	19/2250	1	2	80	86
Other 1:1 trials*	76/4546	117/4588	13/4136	36/4176	6	4	130	137
2:1 or 3:1 trials*	15/1103	11/401	0/941	0/351	1	0	6	3
Totals: all trials	105/7879	147/7239	19/7307	55/6777	8	6	216	226
No. of randomized patients for whom data were not available	224	245	796	707				
Statistical calculations: heparin group†								
O − E no. of events	−28.1		−18.5		+0.8		−8.0	
Variance of O − E	55.2		18.2		3.4		100.6	
Z (P value)	3.8 (<0.0005)		4.3 (<0.0001)		0.4 (NS)		0.8 (NS)	
Typical % reduction in odds (±SD)	40±11		64±15					

Collins, NEJM 1988

Heparin Induced Thrombocytopenia

- Rare if treated < 4 days
- Meta-analysis
  - 15 studies (1984-2004)
  - 7287 patients
- Risk of HIT
  - unfractionated heparin **2.6%**
  - low molecular weight heparin: **0.2%**

Martel, **Blood** 2005

Current Available Guidelines

- American College of Chest Physicians (ACCP)
- American College of Obstetricians and Gynecologists (ACOG)
- Royal College of Obstetricians and Gynecologists (RCOG)
- Society of Obstetricians and Gynecologists of Canada (SOGC)
- Collège National des Gynécologues et Obstétriciens Français (CNGOF)

Variation in Guidelines

ACOG	high-risk thrombophilia, prior VTE, or low-risk thrombophilia with family history of events.	**1%**
ACCP	BMI >30 kg/m2, multiple pregnancy emergency caesarean, smoking. fetal growth restriction	**35%**
RCOG	Prolonged admission, major medical co-morbidities (heart/ lung disease, SLE, cancer, inflammatory conditions, nephrotic syndrome, sickle cell disease, intravenous drug user Age >35, Parity ≥3, surgical procedure Gross varicose veins	**85%**

Palmerola, BJOG 2015

	ACCP			
athy, sickle cell, current IVDU)				

	ACCP			
d by ART				

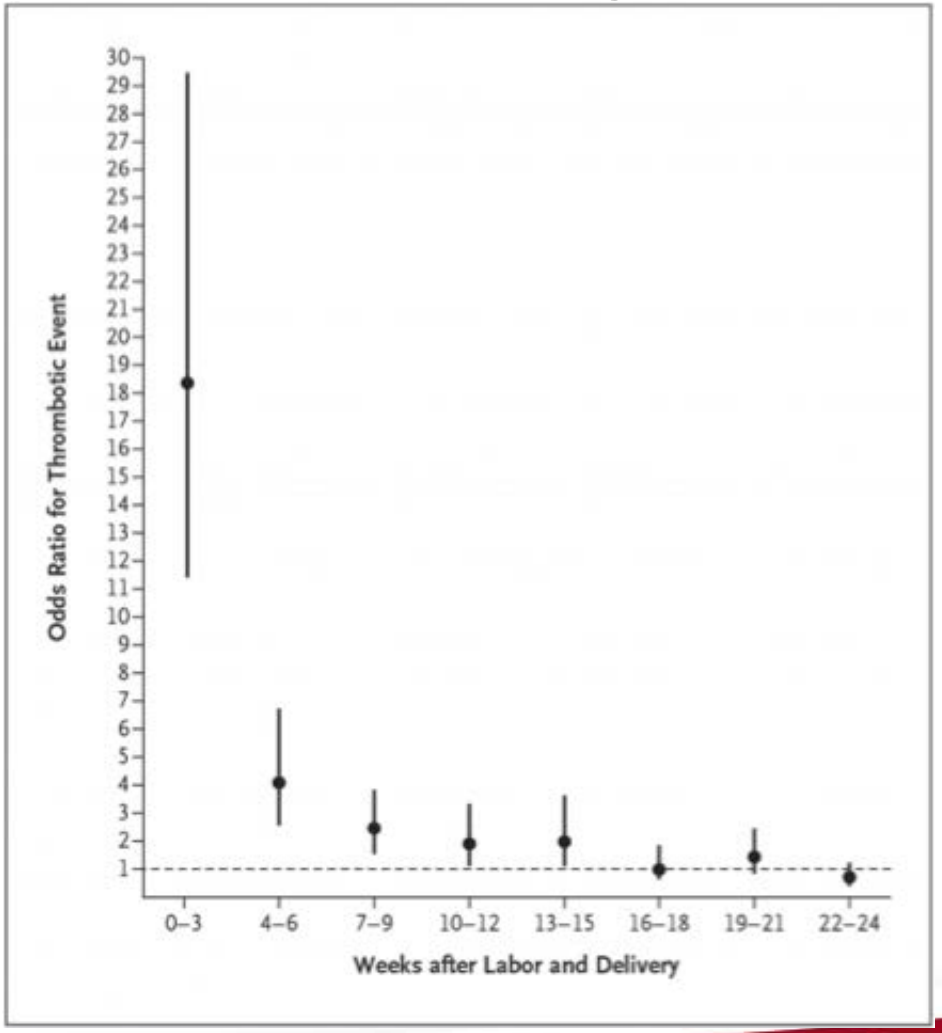
University of Utah Guidelines

- **Major (require 1 major risk factor)**
  - History of VTE
  - High-risk thrombophilia
    - APS (with prior thrombosis)
    - AT III deficiency
    - Homozygous factor V Leiden
    - Homozygous G20210A prothrombin gene mutation
    - Compound heterozygous for factor V Leiden and prothrombin gene mutation
  - Medical comorbdities (i.e. heart disease, SLE, IBD, sickle cell disease, etc)
  - Nephrotic range proteinuria (> 6g, either intrinsic renal disease or preeclampsia-related)
  - Cesarean hysterectomy

University of Utah Guidelines

- **Minor (require ≥ 2 minor risk factors)**
  - BMI >30
  - Multiple pregnancy
  - PPH >1L
  - Smoking >10 cig/d
  - Preeclampsia
  - Emergency cesarean or cesarean in labor
  - Infection: sepsis or triple I around time of delivery
  - Preterm delivery <37 weeks
  - Low-risk thrombophilia
    - Heterozygous factor V Leiden mutation
    - Heterozygous G20210A prothrombin gene mutation
    - Protein C or S deficiency

Timing of thrombotic events after delivery



Kamel, **NEJM** 2014

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Prophylaxis Regimen

- Duration
  - In patient (or 2 weeks for c-hyst)
  - Start 6 hours post-op
- Regimen
  - First Line: enoxaparin (LOVENOX) injection
    - BMI <40: 40mg, Subcutaneous, every 24 hours
    - BMI >40: 30mg, Subcutaneous, every 12 hours
  - Second Line: heparin injection
    - BMI <40: 5,000 units, Subcutaneous, Every 8 hours
    - BMI >40: 7,500 Units, Subcutaneous, Every 8 hours

Summary

- Evaluate every obstetric patient for thromboembolic risk
- All patients undergoing c/s should have SCDs
- Patients with 1 major or 2 minor risk factors should receive pharmacologic DVT prophylaxis