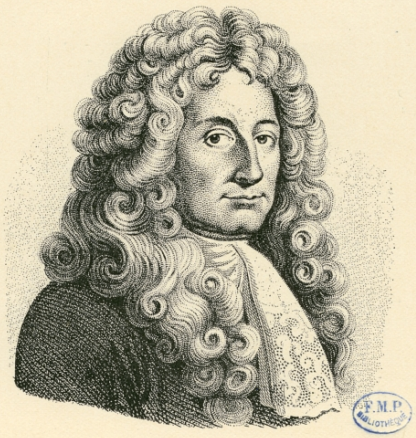
Thromboembolic disease and pregnancy

Sue Robinson

Haematology Consultant

Guy's and St Thomas' NHS
NHS Foundation Trust

1718-First description



FRANCIS MAURICEAU.

This eminent French accoucheur, was born in Paris, in 1637; where we are told that he applied himself with great industry to the study and practice of surgery, especially in the great Hotel-Dieu, for many years before he commenced public practice; so that he rose almost at once to the head of his profession.

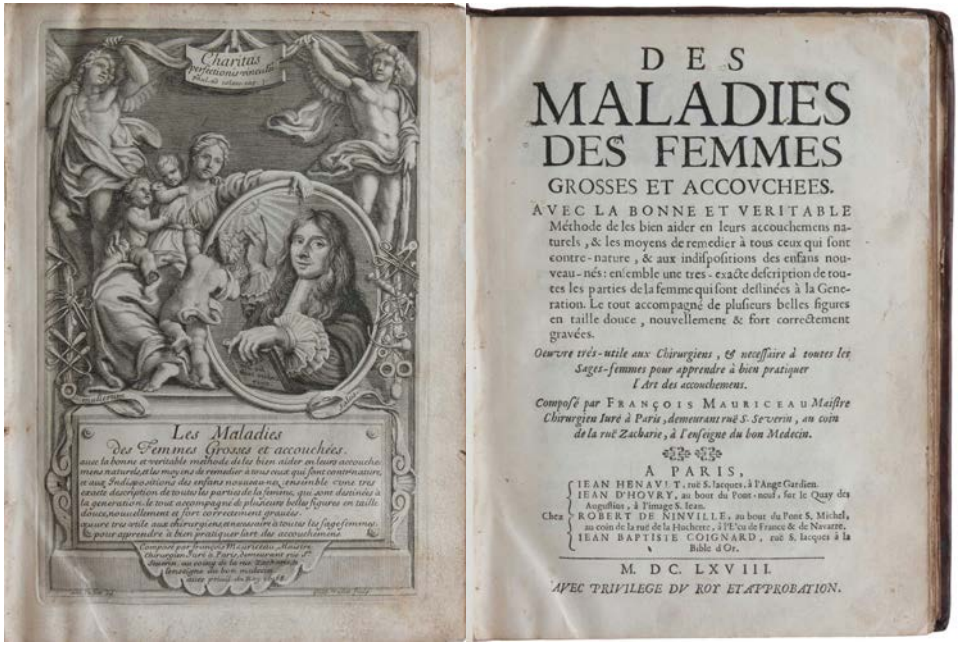
For forty years Mauriceau practiced midwifery in Paris, and he considered no department of medicine or surgery superior to it in dignity and utility. At this period and for more than a century after Mauriceau's death, it was generally regarded as beneath the dignity of a physician to practice this branch of our profession; indeed during the first quarter of the present century, the Royal College of Physicians in London did not admit as a fellow any man who practiced midwifery. His reputation was farther increased by his writings, and maintained by his prudent conduct, and acknowledged skill, during a long series of years; after which he quitted practice entirely, and retired into the country, where he died at an advanced age, in 1709.

He was the first to confine his patients in bed—a bold innovation, as the obstetric chair was looked upon as the only proper place for a confinement. Accoucheurs were engaged in endeavoring to perfect the obstetric chair, very much as their successors of the present day are experimenting and striving to perfect the forceps; and styles and patterns of the "sella lochœa obstetricia seu obstetrica" were as varied as the modern instrument. It has been said that the advent of the obstetric chair marked an era in the history of the art; and it may be as well said that the abandonment of it marked another, to be so soon followed by the great epoch which is marked by the invention of the obstetric forceps. A fourth epoch was begun when anæsthesia was introduced.

For twenty-five years he preserved faithful histories of all the important cases which came under his care, and out of 3,000 he selected 700 of the most important for publication. He published his great work "Traité des Maladies des Femmes grosses, et de celles qui sont accouchées, in 1688, at Paris.

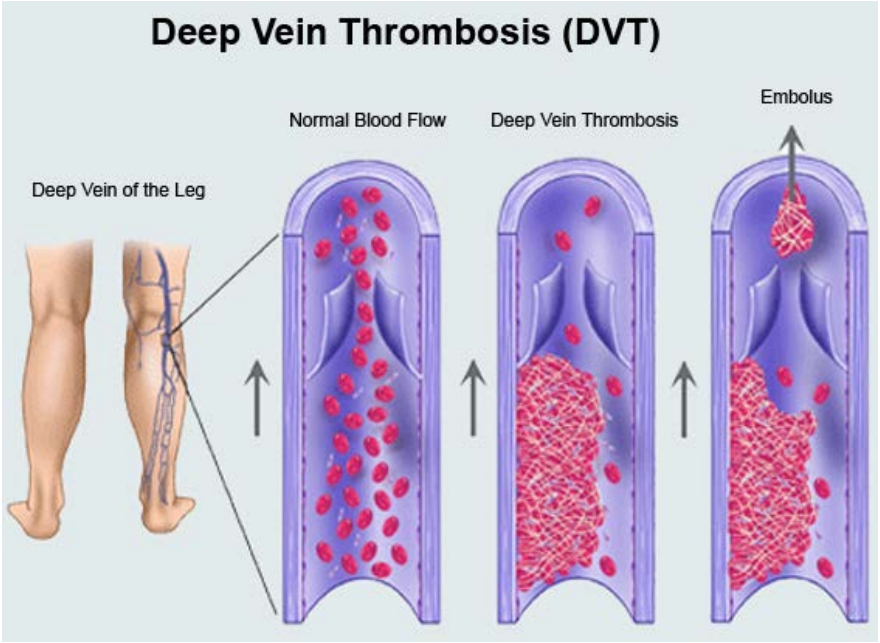
In this work which was so well received that it was soon published in most of the languages which had a medical literature; and was often reprinted both in French and Latin at home; his description of the anatomy of the parts involved in labor is good. He treats of the pregnant state and the diseases connected with it, and then takes up the subject of labor. He recommends version in difficult cases, but is at a loss how to extricate the head when fixed in the pelvis; advocating the use of fillets, and the opening of the head with a spear-shaped knife to allow the introduction of his "*Tirefete*" which seems to have consisted of two metal disks, one of which was to be introduced through the incision in the child's cranium, and the other was to be forced against the exterior of the cranium by means of a long screw which also served as a handle by which traction was made. In his third book, he considers the diseases of the puerperal period and of children. It is chiefly valued by the physicians of to-day, for the larger number of cases which he describes with painstaking accuracy. The writer's library contains the fine quarto edition of his works which were collected and published in two volumes, at Paris, after his death in 1712.

J. H. H.



Thromboembolic disease

- Venous thrombosis = fibrin and red cells
- Originate in areas of sluggish blood flow
- Propagate in the absence of antithrombotic therapy
- Risk of Embolisation



Symptoms and Signs deep vein thrombosis (DVT)

- Leg pain
- Tenderness
- Swelling
- Warmth
- Discoloration
- Lower abdominal pain
- Increased temperature

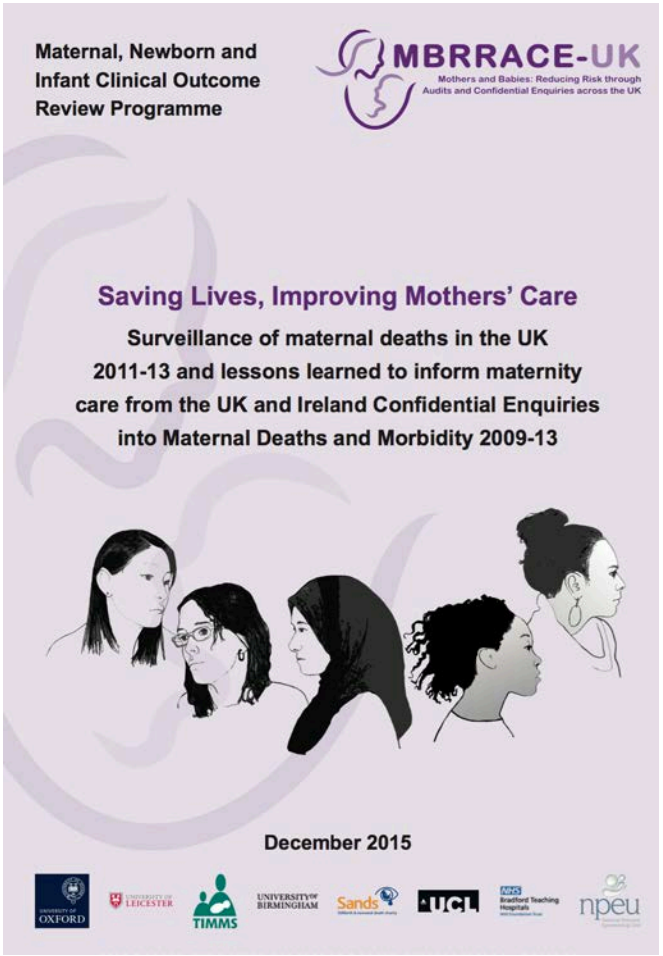
Symptoms and Signs Pulmonary Embolus (PE)

- Chest pain
- Shortness of breath
- Coughing up blood
- Fast pulse
- Raised venous pressure
- Collapse

Incidence of venous thrombosis

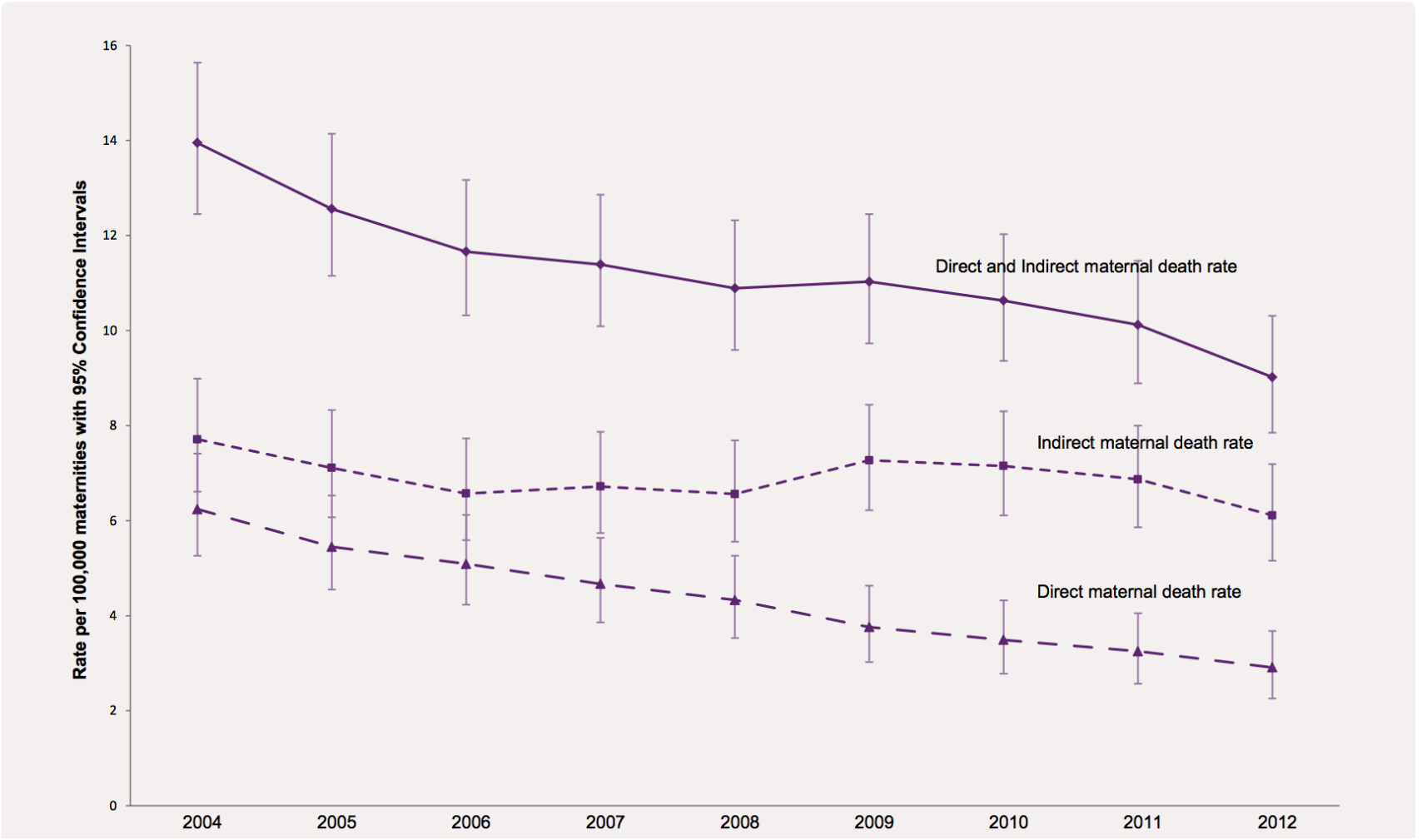
Incidence of venous thrombosis

Maternal Mortality data



Maternal death rate 2004-12

(Three year rolling averages)



Maternal Mortality Data

Table 2.5: UK Maternal deaths and mortality rates by cause 1985–2011

Cause of death	Numbers									Rates per 100,000 maternities								
	1985–87	1988–90	1991–93	1994–96	1997–99	2000–02	2003–05	2006–08	2009–11	1985–87	1988–90	1991–93	1994–96	1997–99	2000–02	2003–05	2006–08	2009–11
All Direct and Indirect deaths	223	238	228	268	242	261	295	261	252	9.83	10.08	9.85	12.19	11.4	13.07	13.95	11.39	10.63
Direct deaths																		
Genital tract sepsis*	9	17	15	16	18	13	18	26	14	0.40	0.72	0.65	0.73	0.85	0.65	0.85	1.13	0.63
Pre-eclampsia and eclampsia	27	27	20	20	16	14	18	19	10	1.19	1.14	0.86	0.91	0.75	0.70	0.85	0.83	0.42
Thrombosis and thromboembolism	32	33	35	48	35	30	41	18	30	1.41	1.40	1.51	2.18	1.65	1.50	1.94	0.79	1.26
Amniotic fluid embolism	9	11	10	17	8	5	17	13	7	0.40	0.47	0.43	0.77	0.38	0.25	0.80	0.57	0.29
Early pregnancy deaths	16	24	17	15	17	15	14	11	4	0.71	1.02	0.73	0.68	0.80	0.75	0.66	0.48	0.17
Haemorrhage	10	22	15	12	7	17	14	9	14	0.44	0.93	0.65	0.55	0.33	0.85	0.66	0.39	0.59
Anaesthesia	6	4	8	1	3	6	6	7	3	0.26	0.17	0.35	0.05	0.14	0.30	0.28	0.31	0.12
Other Direct‡	27	17	14	7	7	8	4	4	0	1.19	0.72	0.60	0.32	0.33	0.40	0.19	0.17	–
All direct	139	145	128	134	106	106	132	107	82	6.13	6.14	5.53	6.10	4.99	5.31	6.24	4.67	3.49
Indirect deaths																		
Cardiac disease	23	18	37	39	35	44	48	53	51	1.01	0.76	1.60	1.77	1.65	2.20	2.27	2.31	2.14
Other Indirect causes	43	45	38	39	41	50	50	49	72	1.90	1.91	1.64	1.77	1.93	2.50	2.37	2.14	3.03
Indirect neurological conditions	19	30	25	47	34	40	37	36	30	0.84	1.27	1.08	2.14	1.60	2.00	1.75	1.57	1.26
Psychiatric causes	†	†	†	9	15	16	18	13	13	†	†	†	0.41	0.71	0.80	0.85	0.57	0.55
Indirect malignancies	†	†	†	†	11	5	10	3	4	†	†	†	†	0.52	0.25	0.47	0.13	0.17
All Indirect	84	93	100	134	136	155	163	154	170	3.70	3.94	4.32	6.10	6.40	7.76	7.71	6.59	7.15
Coincidental	26	39	46	36	29	36	55	50	22	1.15	1.65	1.99	1.64	1.37	1.80	2.60	2.18	0.98

*Including early pregnancy deaths as a result of sepsis

‡Acute fatty liver and genital tract trauma; included with pre-eclampsia and eclampsia and haemorrhage respectively from 2009 onwards

†Deaths from these causes not included in reports from earlier years

Source: CMACE, MBRRACE-UK

Maternal Mortality Data

Cause of death	2009-11			2010-12			2011-13		
	n	Rate	95% CI	n	Rate	95% CI	n	Rate	95% CI
All Direct and Indirect deaths	253	10.63	9.36–12.03	243	10.12	8.89–11.47	214	9.02	7.85–10.31
Direct deaths									
*Sepsis**	15	0.63	0.35–1.04	12	0.50	0.26–0.87	7	0.29	0.12–0.61
Pre-eclampsia and eclampsia	10	0.42	0.2–0.77	9	0.38	0.18–0.71	6	0.25	0.09–0.55
Thrombosis and thromboembolism	30	1.26	0.85–1.80	26	1.08	0.71–1.59	24	1.01	0.65–1.5
Amniotic fluid embolism	7	0.29	0.12–0.61	8	0.33	0.14–0.66	10	0.42	0.20–0.78
Early pregnancy deaths	4	0.17	0.05–0.43	8	0.33	0.14–0.66	6	0.25	0.09–0.55
Haemorrhage	14	0.59	0.32–0.99	11	0.46	0.23–0.82	13	0.55	0.29–0.94
Anaesthesia	3	0.12	0.03–0.37	4	0.17	0.05–0.43	3	0.13	0.03–0.37
All Direct	83	3.49	2.78–4.32	78	3.25	2.57–4.05	69	2.91	2.26–3.68
Indirect									
Cardiac disease	51	2.14	1.60–2.82	54	2.25	1.69–2.93	49	2.06	1.53–2.73
Indirect Sepsis - Influenza	27	1.13	0.75–1.65	13	0.54	0.29–0.93	9	0.38	0.17–0.72
Indirect Sepsis – Pneumonia/ others	16	0.67	0.38–1.09	22	0.92	0.57–1.39	21	0.89	0.55–1.35
Other Indirect causes	29	1.22	0.82–1.75	26	1.08	0.71–1.59	22	0.93	0.58–1.40
Indirect neurological conditions	30	1.26	0.85–1.80	31	1.29	0.88–1.83	24	1.01	0.65–1.50
Psychiatric causes	13	0.55	0.29–0.93	16	0.67	0.38–1.08	19	0.80	0.48–1.25
Indirect malignancies	4	0.17	0.05–0.45	3	0.13	0.03–0.37	1	0.04	0.001–0.24
All Indirect	170	7.15	6.11–8.30	165	6.87	5.86–8.00	145	6.11	5.16–7.19
Coincidental deaths	23	0.98	0.61–1.45	26	1.08	0.71–1.59	26	1.10	0.72–1.61
Late deaths	325	13.66	12.22–15.33	313	13.03	11.63–14.56	335	14.12	12.64–15.71

Implementation guidelines

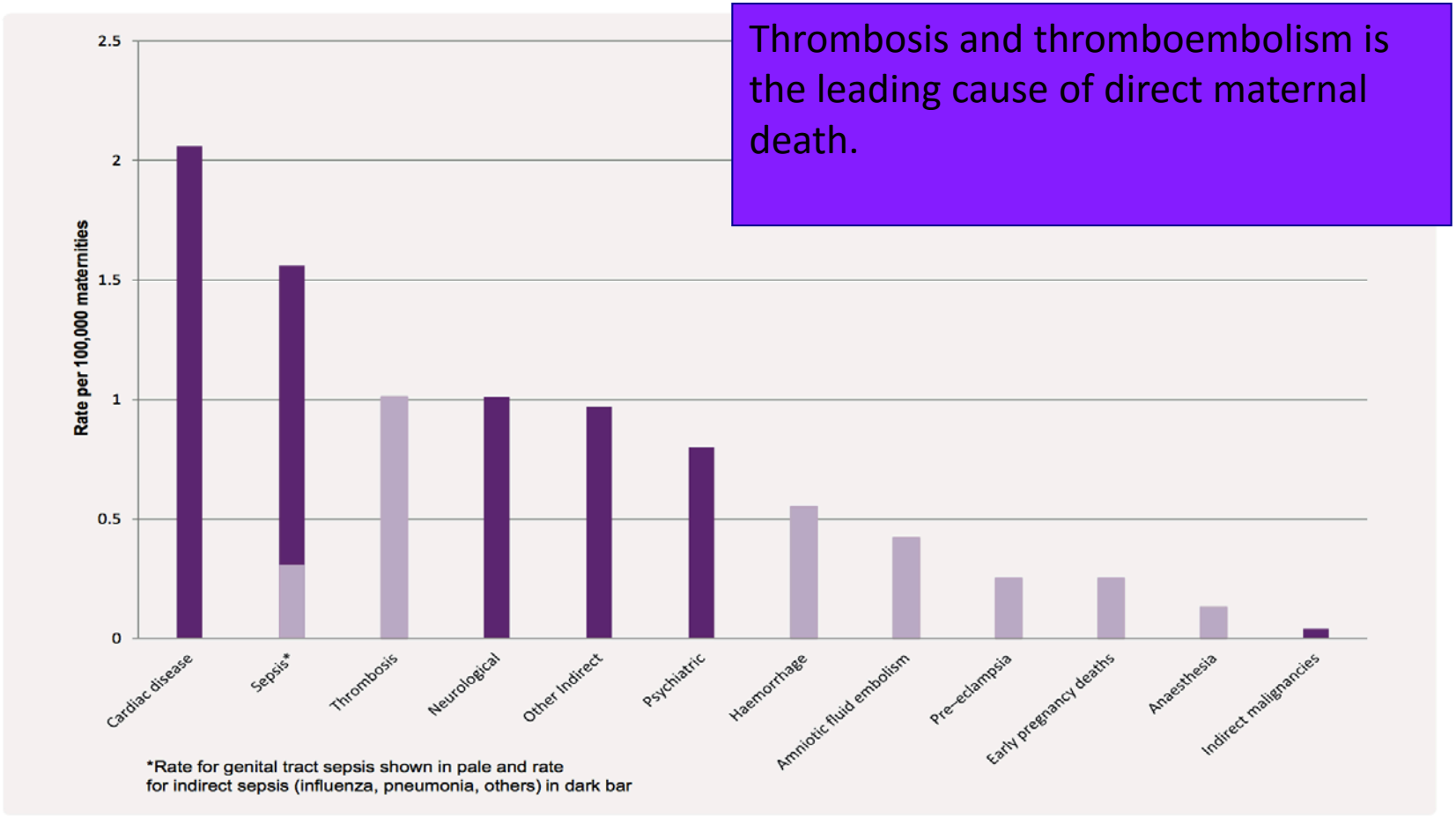
Recognition Risk

Compliance

Demographics

Causes of maternal death

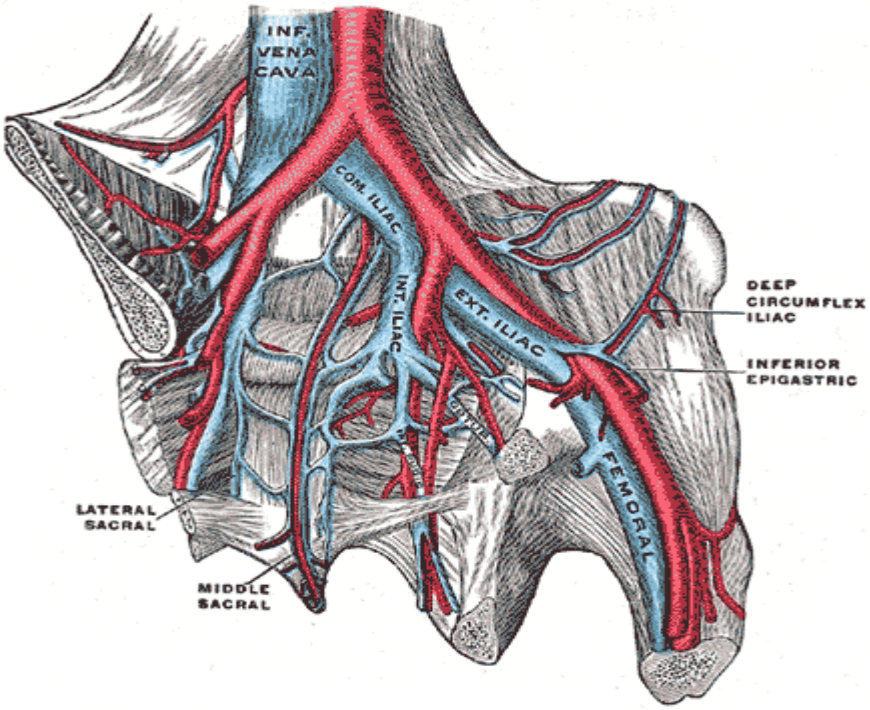
Thrombosis and thromboembolism is the leading cause of direct maternal death.



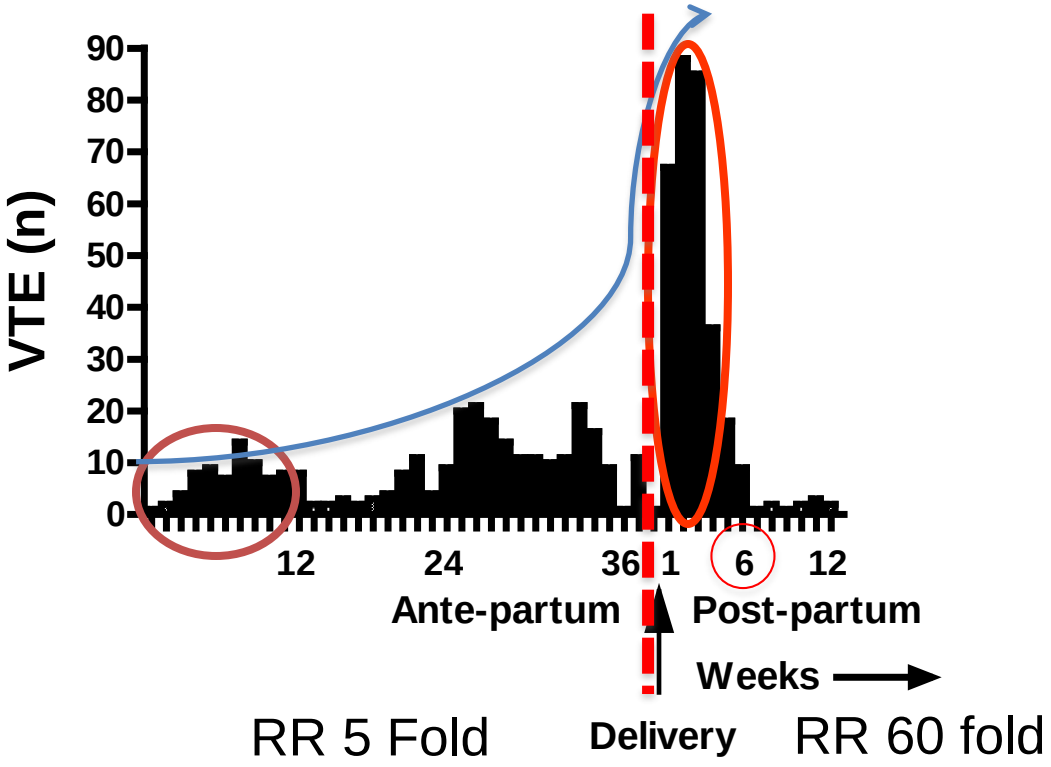
Venous thrombosis in pregnancy

70% arise in proximal iliac and femoral veins (9% outside pregnancy)

90% of DVT occur in the left leg in pregnancy (55% outside pregnancy)



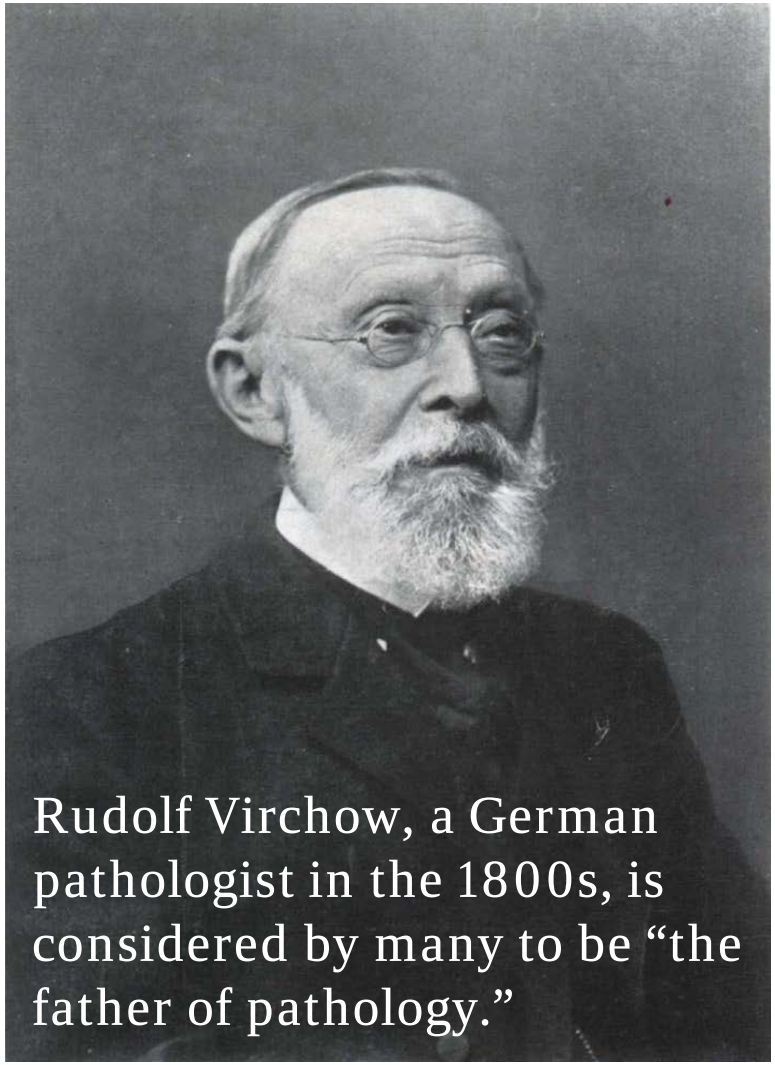
Distribution of venous thromboembolism (VTE)in pregnancy and puerperium



AJOG, 2008;198:233.e1-233.e7 ,AF Jacobsen, FE Skjeldestad, PM Sandset,

Incidence and risk patterns of VTE in pregnancy and puerperium

Risk Factors for venous thromboembolism



- Alteration in normal blood flow (stasis)
- 50% reduction in blood flow to lower limbs by 29 weeks
- Trauma or damage to the vascular endothelium
- During vaginal or abdominal delivery
- Alteration in the constitution of blood (hypercoagulability)
- Increased levels factor VIII, fibrinogen, reduced levels protein S, resistance to activated protein C and impaired fibrinolysis

Risk Factors for pregnancy related venous thromboembolism

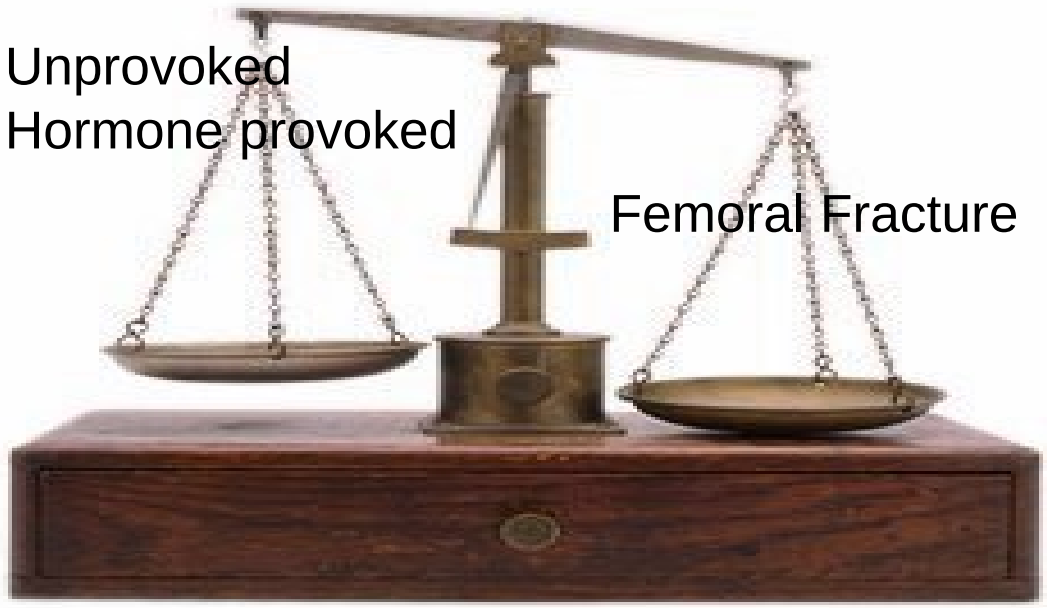
Pre-existing	Previous VTE	
	Thrombophilia	*Heritable* Antithrombin deficiency Protein C deficiency Protein S deficiency Factor V Leiden Prothrombin gene mutation
		Acquired Antiphospholipid antibodies Persistent lupus anticoagulant and/or persistent moderate/high titre anticardiolipin antibodies and/or β_2-glycoprotein 1 antibodies
	Medical comorbidities e.g. cancer; heart failure; active SLE, inflammatory polyarthropathy or IBD; nephrotic syndrome; type I diabetes mellitus with nephropathy; sickle cell disease;[58] current intravenous drug user	
	Age > 35 years	
	Obesity (BMI ≥ 30 kg/ m²) either prepregnancy or in early pregnancy	
	Parity ≥ 3 (a woman becomes para 3 after her third delivery)	
	Smoking	
	Gross varicose veins (symptomatic or above knee or with associated phlebitis, oedema/skin changes)	
	Paraplegia	
Obstetric risk factors	Multiple pregnancy Current pre-eclampsia	
	Caesarean section Prolonged labour (> 24 hours) Mid-cavity or rotational operative delivery Stillbirth Preterm birth Postpartum haemorrhage (> 1 litre/ requiring transfusion)	
New onset/transient *These risk factors are potentially reversible and may develop at later stages in gestation than the initial risk assessment or may resolve and therefore what is important is an ongoing individual risk assessment*	Any surgical procedure in pregnancy or puerperium except immediate repair of the perineum, e.g. appendicectomy, postpartum sterilisation Bone fracture	
	Hyperemesis, dehydration	
	Ovarian hyperstimulation syndrome (first trimester only)	Assisted reproductive technology (ART), in vitro fertilisation (IVF)
	Admission or immobility (≥ 3 days' bed rest)	e.g. pelvic girdle pain restricting mobility
	Current systemic infection (requiring intravenous antibiotics or admission to hospital)	e.g. pneumonia, pyelonephritis, postpartum wound infection
	Long-distance travel (> 4 hours)	

Maternal risk Factors

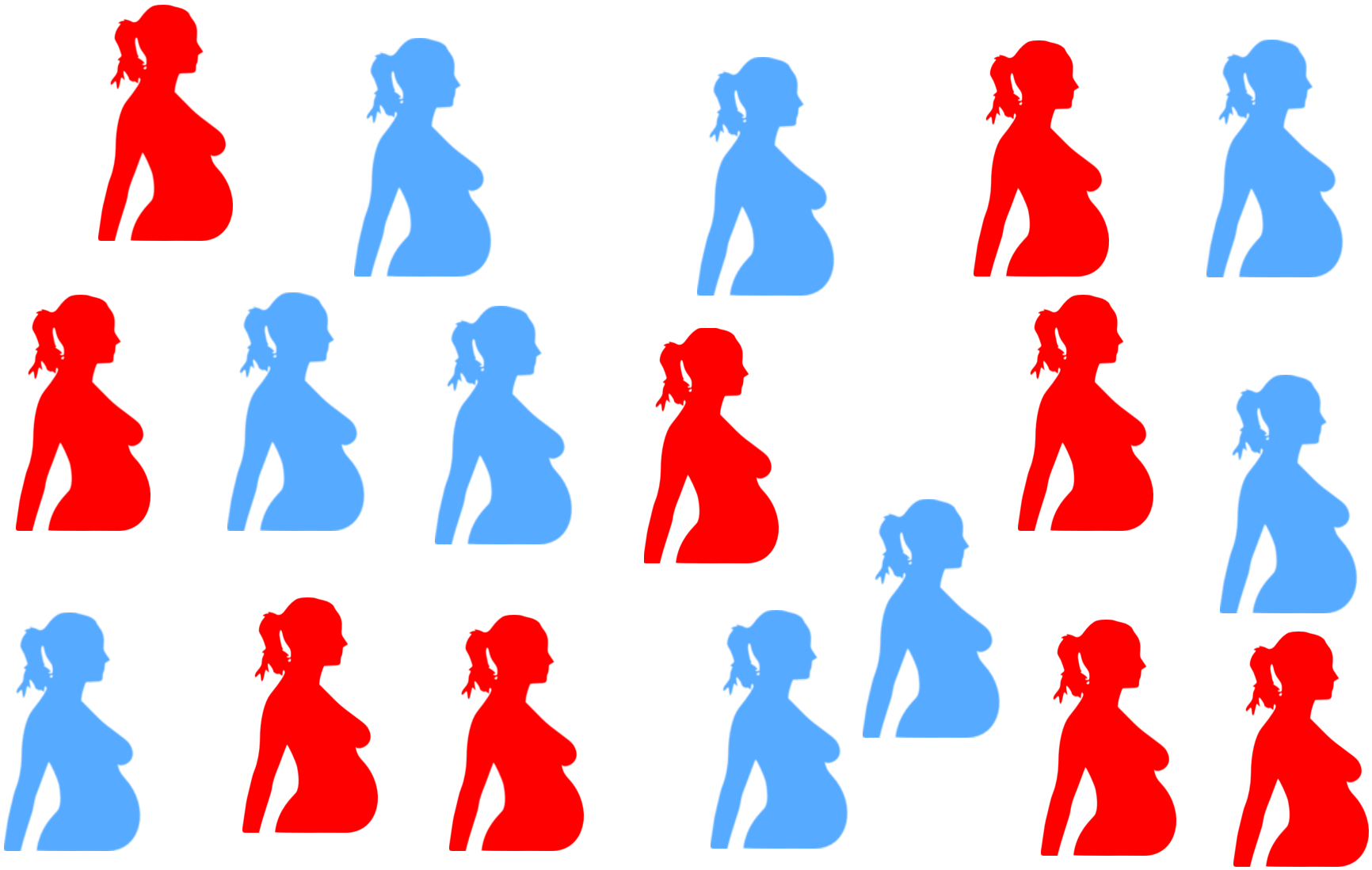
- Personal history VTE
- Thrombophilia
- Family and personal history of VTE
- Obesity
- Age and Parity

Previous VTE

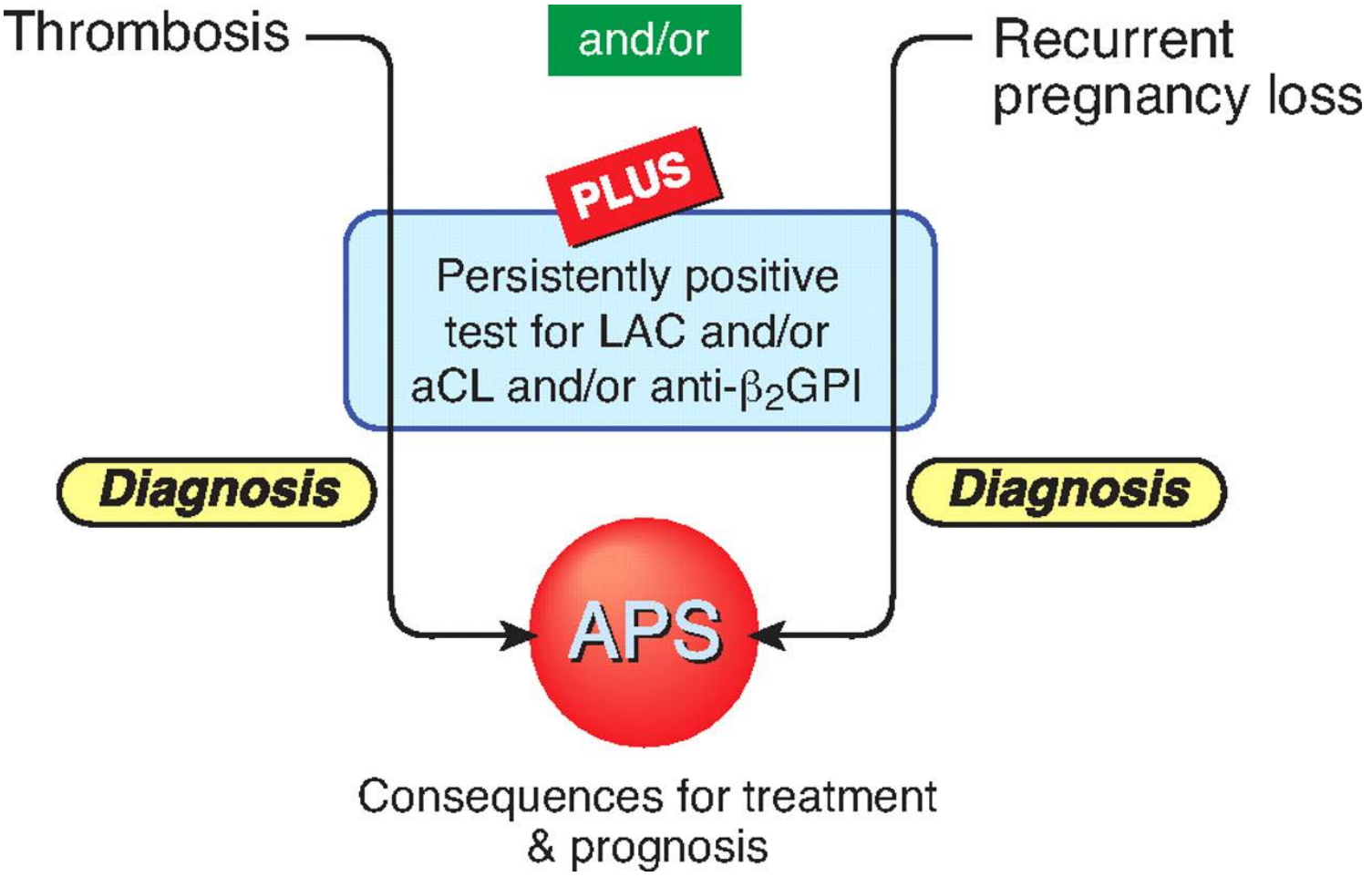
- Pregnancy increases risk of recurrence 3-4 fold
- 15-25% of pregnancy related thrombosis are recurrent events



Thrombophilia



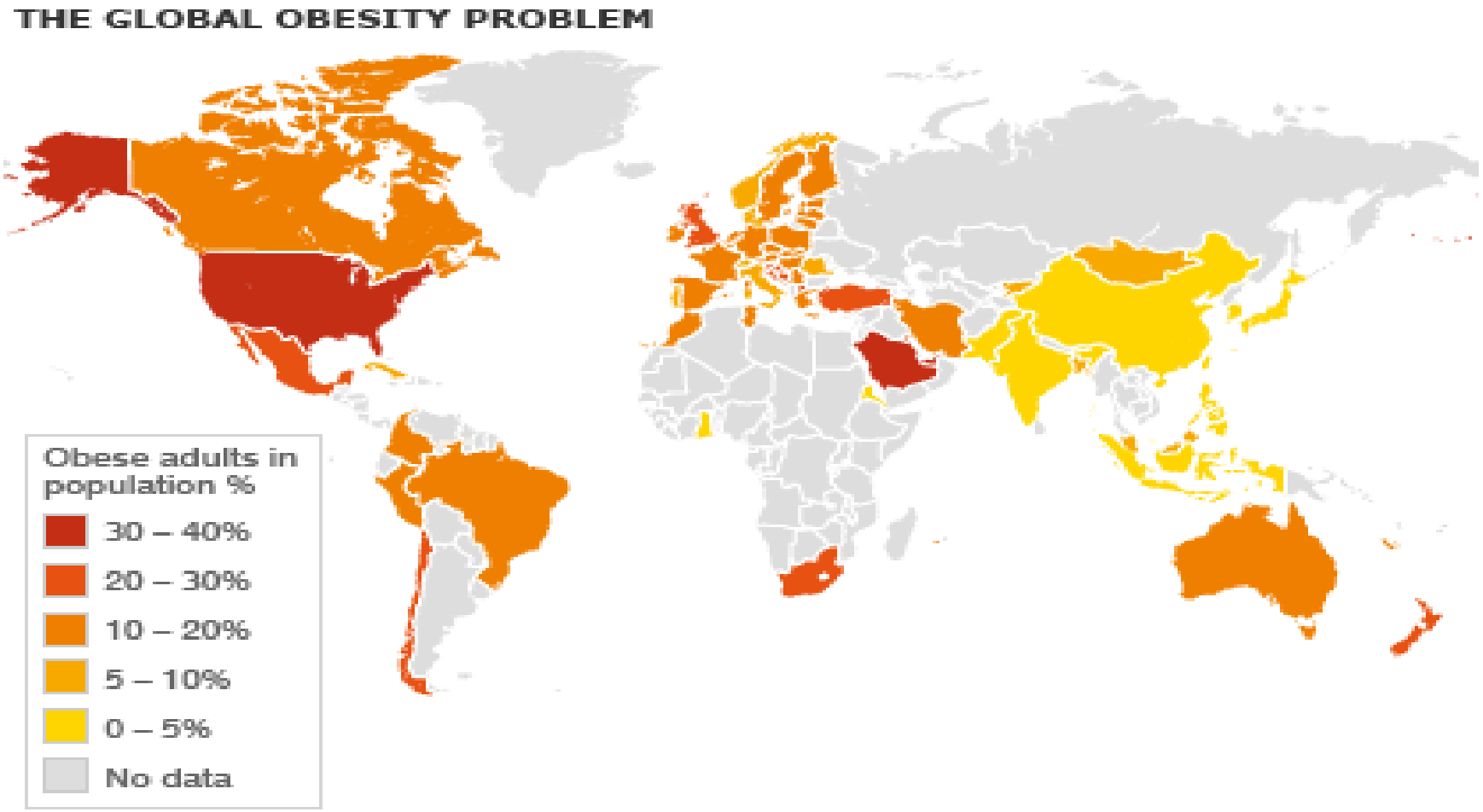
Acquired thrombophilia



Bill Giannakopoulos et al. Blood 2009;113:985-994

blood

Obesity


THE GLOBAL OBESITY PROBLEM
Obese adults in population %
30 – 40%
20 – 30%
10 – 20%
5 – 10%
0 – 5%
No data
An obese adult is classified as having a Body Mass Index equal to or greater than 30
SOURCE: World Health Organization, 2005

Age and Parity

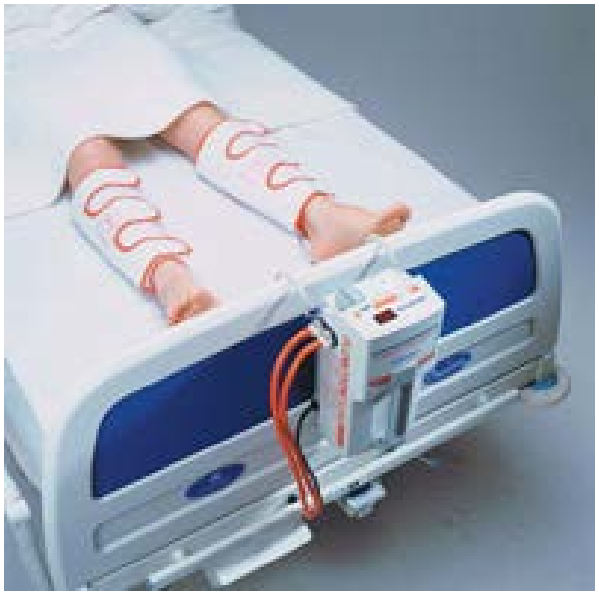
Pregnancy related risk factors

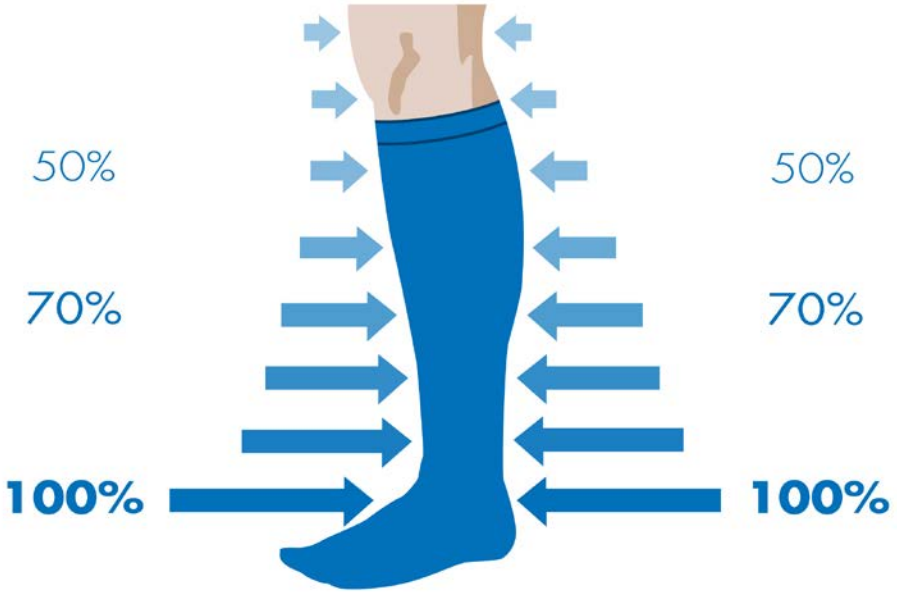
- Preconception – hormone stimulation
- During pregnancy – pre eclampsia
- Mode delivery and complications- blood loss

Vaginal	Elective	Emergency
Delivery	Caesarean	Caesarean

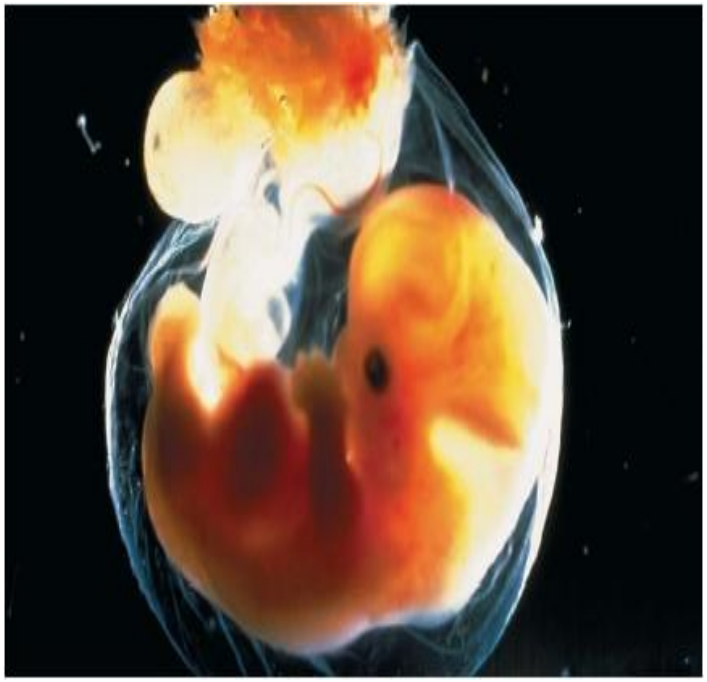
Modalities of thromboprophylaxis

Mechanical Thromboprophylaxis





Pharmacological thromboprophylaxis



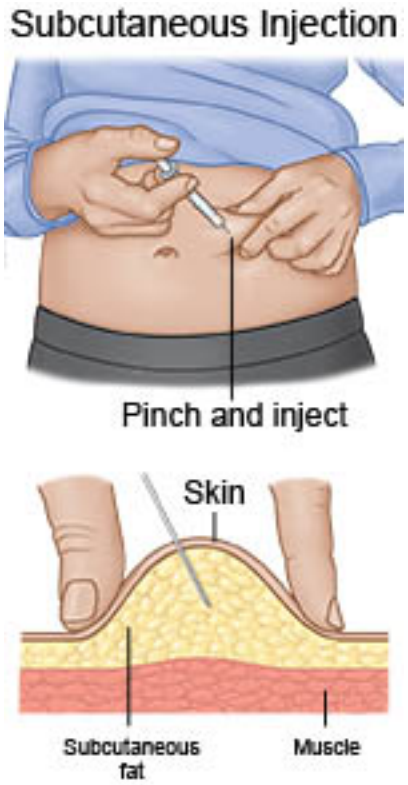
- Low molecular weight heparin
- Does not cross the placenta
- Not secreted into breast milk

(N=2777)

Complications All indications	Complication	Rate %	95% CI	Rate %	95% CI
Thrombosis	VTE	0.86	0.55-	1.37	0.97-1.87
	Recurrence for acute VTE = 2/174 = 1.15%				
	Arterial 14	0.50	0.28-0.84		
Bleeding	Antenatal	0.43	0.22-0.75	1.98	1.50-2.57
	PPH > 500 mls	0.94	0.61-1.37		
	Wound haematoma	0.61	0.36-0.98		
Allergy		1.80		1.80	1.34-2.37
Thrombo-cytopenia	Platelets < 100 x 10^9	0.11		0.11	0.02-0.32
	HIT	0		0	0-0.14
Osteoporosis		0.04		0.04	0.0001-0.2

Greer & Nelson-Piercy. Blood 2005; 106: 401-7

Pharmacological thromboprophylaxis



Subcutaneous prophylactic unfractionated heparin

Catheter placement/Removal >2-4 hours after injection

Delay next dose until >2 hours post insertion

Delay next dose until >4 hours post removal

Intravenous infusion unfractionated heparin

Catheter placement > 4 hours after stopping infusion, APTTr normal

Restart infusion > 2 hours after insertion

Restart infusion > 4 hours after removal

Low molecular weight heparin

Spinal or epidural insertion

>8 hours after last injection – low dose

>12 hours after last injection – intermediate dose

>24 hours after last injection - full anticoagulation

Removal epidural catheter 12 hours after any dose

Delay next dose until 2 hours after insertion

Delay next dose until > 4 hours after removal

Management approach

Royal College of Obstetricians & Gynaecologists

Reducing the Risk of Venous Thromboembolism during Pregnancy and the Puerperium

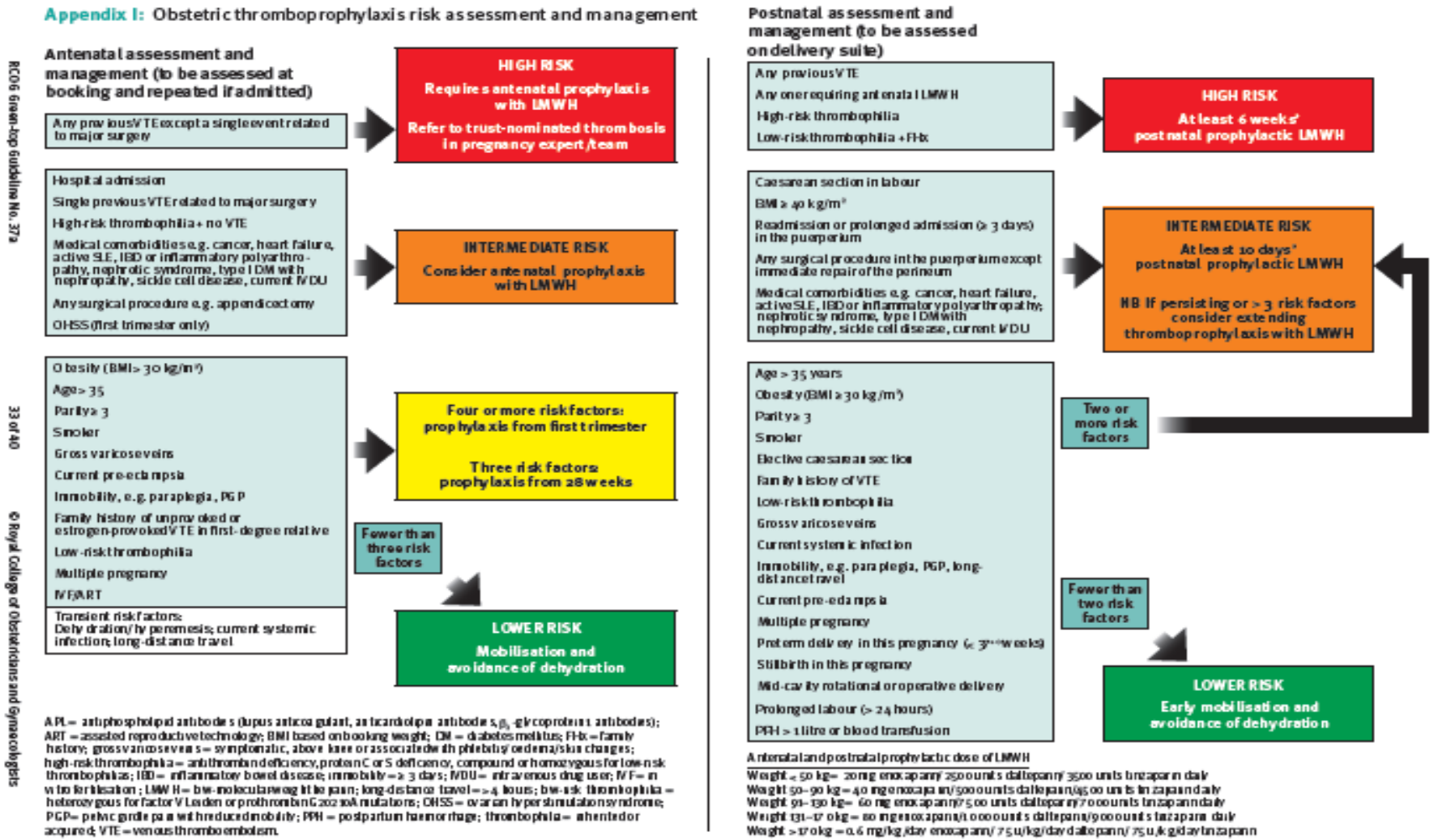
Green-top Guideline No. 37a
April 2015

NICE accredited
www.nice.org.uk/accreditation

Management approach

- At risk women offered thromboprophylaxis
- Lack of standardisation risk factors
- Lack of evidence
- Weight of a risk factor
- Duration based upon number of risk factors

RCOG risk assessment



Risk Assessment

Appendix III: Risk assessment for venous thromboembolism (VTE)

- If total score ≥ 4 antenatally, consider thromboprophylaxis from the first trimester.
- If total score 3 antenatally, consider thromboprophylaxis from 28 weeks.
- If total score ≥ 2 postnatally, consider thromboprophylaxis for at least 10 days.
- If admitted to hospital antenatally consider thromboprophylaxis.
- If prolonged admission (≥ 3 days) or readmission to hospital within the puerperium consider thromboprophylaxis.

For patients with an identified bleeding risk, the balance of risks of bleeding and thrombosis should be discussed in consultation with a haematologist with expertise in thrombosis and bleeding in pregnancy.

Risk factors for VTE

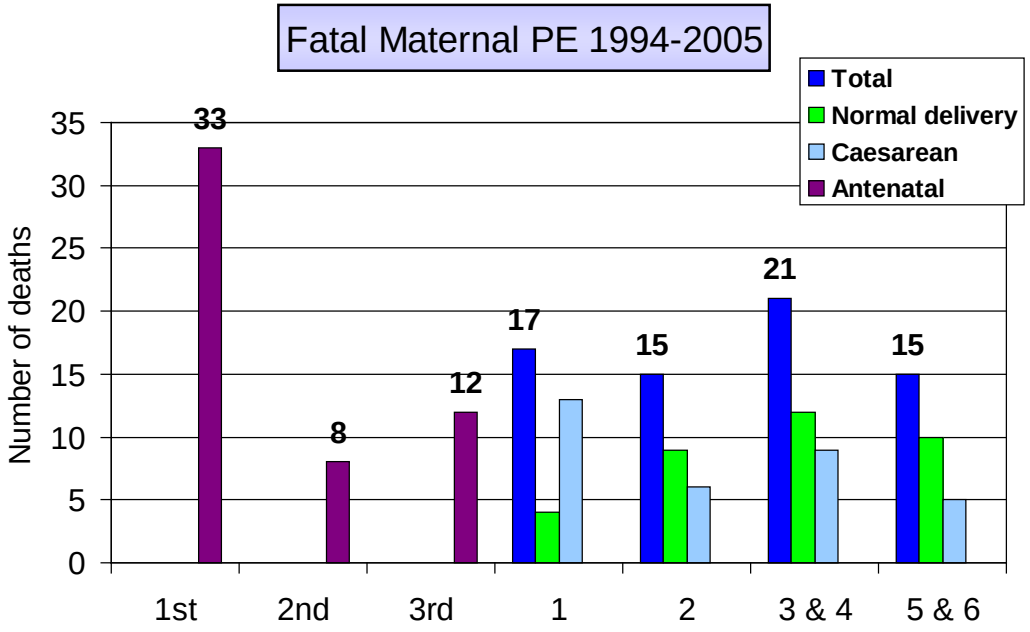
Pre-existing risk factors	Tick	Score
Previous VTE (except a single event related to major surgery)		4
Previous VTE provoked by major surgery		3
Known high-risk thrombophilia		3
Medical comorbidities e.g. cancer, heart failure; active systemic lupus erythematosus, inflammatory polyarthropathy or inflammatory bowel disease; nephrotic syndrome; type I diabetes mellitus with nephropathy; sickle cell disease; current intravenous drug user		3
Family history of unprovoked or estrogen-related VTE in first-degree relative		1
Known low-risk thrombophilia (no VTE)		1[a]
Age (> 35 years)		1
Obesity		1 or 2[b]
Parity ≥ 3		1
Smoker		1
Gross varicose veins		1
Obstetric risk factors		
Pre-eclampsia in current pregnancy		1
ART/IVF (antenatal only)		1
Multiple pregnancy		1
Caesarean section in labour		2
Elective caesarean section		1
Mid-cavity or rotational operative delivery		1
Prolonged labour (> 24 hours)		1
PPH (> 1 litre or transfusion)		1
Preterm birth < 37[+0] weeks in current pregnancy		1
Stillbirth in current pregnancy		1
Transient risk factors		
Any surgical procedure in pregnancy or puerperium except immediate repair of the perineum, e.g. appendicectomy, postpartum sterilisation		3
Hyperemesis		3
OHSS (first trimester only)		4
Current systemic infection		1
Immobility, dehydration		1
TOTAL		

Antenatal thromboprophylaxis

- Previous VTE - LMWH from early
- Four risk factors - LMWH throughout
- Three risk factors - LMWH from 28 weeks
- Admission – LMWH unless contraindications / bleeding
- First trimester

-OHSS – LMWH for T1

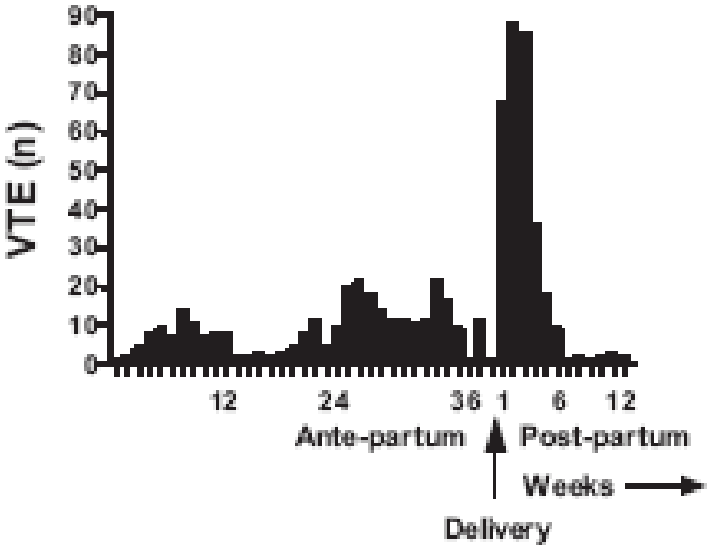
-IVF – LMWH if 3 other risk factors



Women receiving LMWH antenatally should continue prophylactic doses of LMWH until six weeks post partum.

FIGURE 2

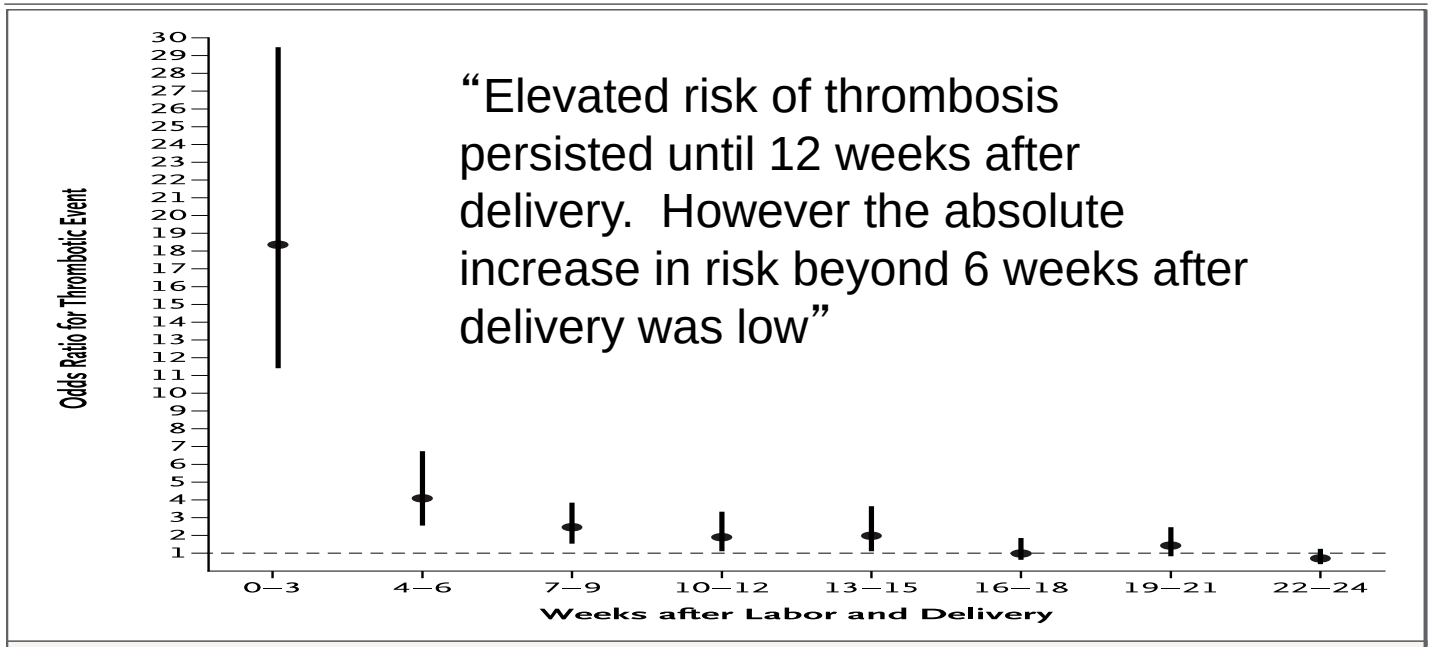
Distribution of VTE in pregnancy and puerperium



Number of VTEs per week.

Jacobsen. Incidence and risk patterns of venous thromboembolism in pregnancy and puerperium. Am J Obstet Gynecol 2008.

Postpartum thromboprophylaxis



"Elevated risk of thrombosis persisted until 12 weeks after delivery. However the absolute increase in risk beyond 6 weeks after delivery was low"

Postpartum Thromboprophylaxis

All previous VTE 6 weeks

- All emergency Caesarean section 10 days
- Any woman with 2 risk factors including:
  - Caesarean Section
  - PPH / transfusion
  - Infection
  - Stillbirth
  - Preterm labour

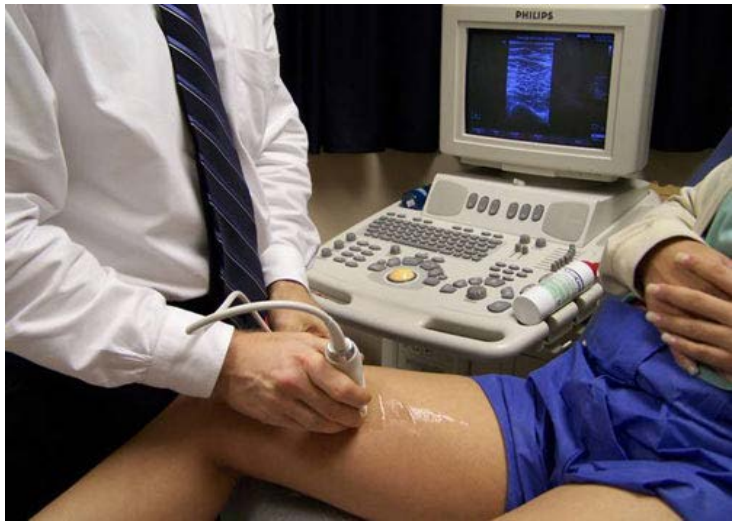
Management approach

- Mutidisciplinary approach
- High risk women
- Uncertainty regarding risk
- Refer to obstetric haematology clinic
- Risk stratification
- Reviewed and risk assessed regular intervals

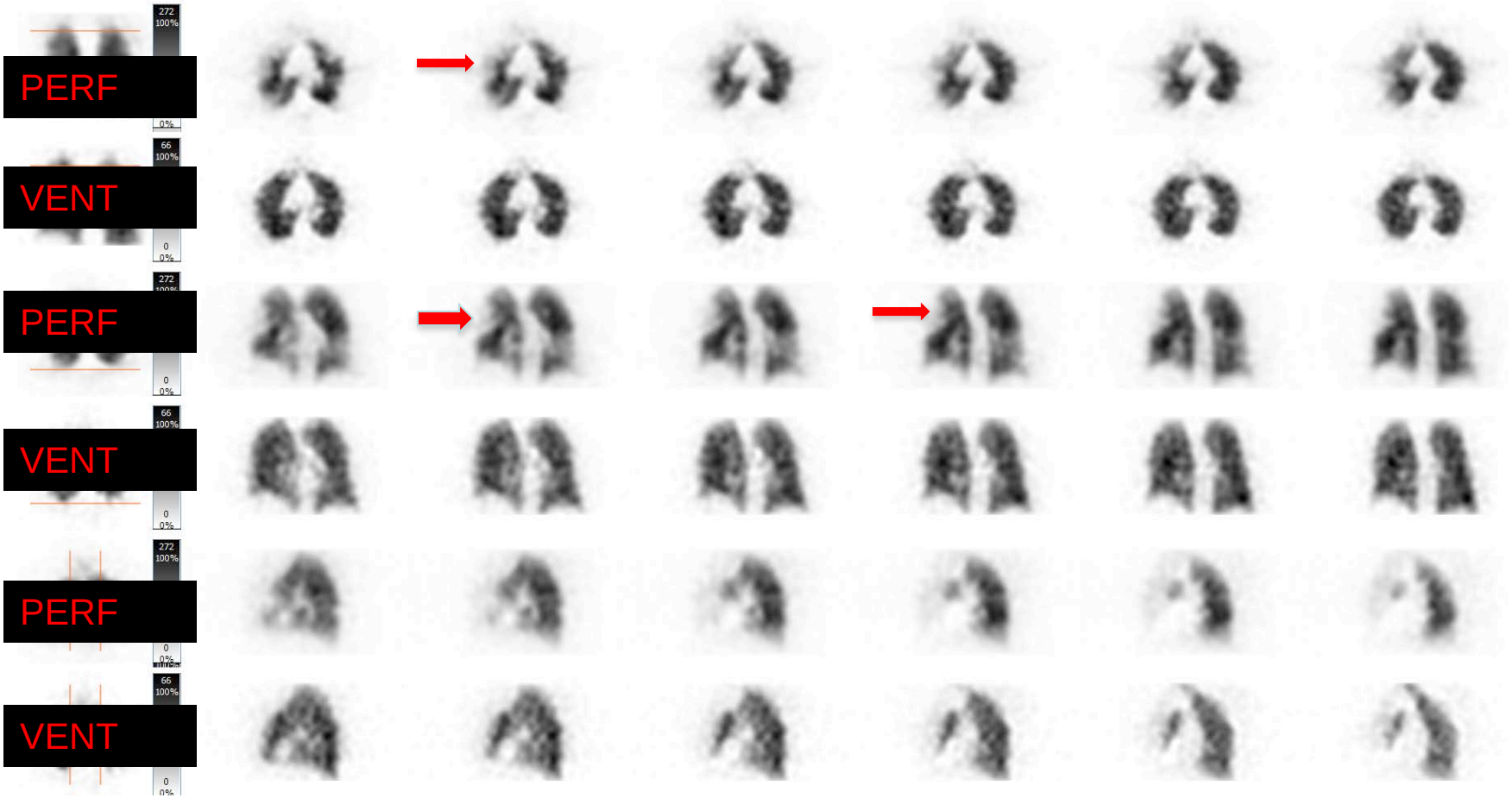
Diagnosis of DVT

Compression duplex ultrasound

- A normal ultrasound does not exclude a calf DVT
- If high index of suspicion
- Maintain anticoagulation
- Rescan



VQ SPECT



Treatment dose

Weight	**Enoxaparin**	**Dalteparin**	**Tinzaparin** (75u/kg/day)
<50kg	20mg daily	2500 units daily	3500 units daily
50-90kg	40mg daily	5000 units daily	4500 units daily
91-130kg	60 mg daily*	7500 units daily*	7000units daily*
131-170kg	80 mg daily*	10000 units daily*	9000 units daily*
>170kg	0.6mg/kg/day*	75u/kg/day*	75u/kg/day*
High prophylactic (intermediate) dose for women weighing 50-90kg	40mg 12 hourly	5000 units 12 hourly	
Treatment dose	1mg/kg/12 hourly antenatal 1.5mg/kg/daily postnatal	100u/kg/12 hourly or 200u/kg/daily postnatal	175u/kg/daily (antenatal and post natal)

Monitoring LMWH

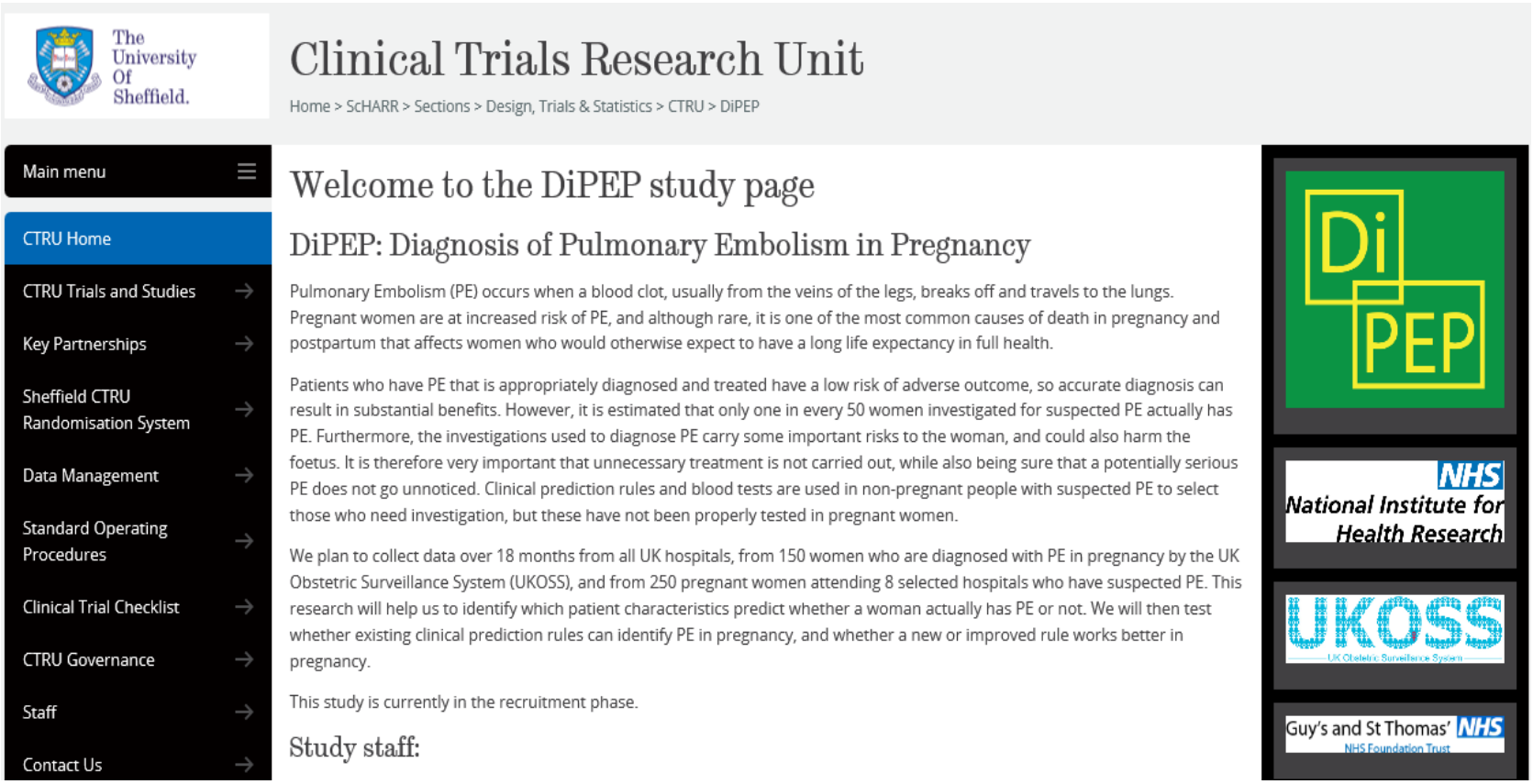
- Not routinely recommended
- Extremes of body weight <50kg, >90kg
- Renal impairment
- Recurrent thrombosis

Post partum anticoagulation

UK Guidance in pregnancy

- Ongoing risk factor
- Safety profile LMWH
- Continue duration pregnancy and 6 weeks post partum
- Duration of treatment at least 3 months

Research


The University Of Sheffield.
Clinical Trials Research Unit
Home > ScHARR > Sections > Design, Trials & Statistics > CTRU > DiPEP
Main menu
CTRU Home
CTRU Trials and Studies
Key Partnerships
Sheffield CTRU Randomisation System
Data Management
Standard Operating Procedures
Clinical Trial Checklist
CTRU Governance
Staff
Contact Us
Welcome to the DiPEP study page
DiPEP: Diagnosis of Pulmonary Embolism in Pregnancy
Pulmonary Embolism (PE) occurs when a blood clot, usually from the veins of the legs, breaks off and travels to the lungs. Pregnant women are at increased risk of PE, and although rare, it is one of the most common causes of death in pregnancy and postpartum that affects women who would otherwise expect to have a long life expectancy in full health.
Patients who have PE that is appropriately diagnosed and treated have a low risk of adverse outcome, so accurate diagnosis can result in substantial benefits. However, it is estimated that only one in every 50 women investigated for suspected PE actually has PE. Furthermore, the investigations used to diagnose PE carry some important risks to the woman, and could also harm the foetus. It is therefore very important that unnecessary treatment is not carried out, while also being sure that a potentially serious PE does not go unnoticed. Clinical prediction rules and blood tests are used in non-pregnant people with suspected PE to select those who need investigation, but these have not been properly tested in pregnant women.
We plan to collect data over 18 months from all UK hospitals, from 150 women who are diagnosed with PE in pregnancy by the UK Obstetric Surveillance System (UKOSS), and from 250 pregnant women attending 8 selected hospitals who have suspected PE. This research will help us to identify which patient characteristics predict whether a woman actually has PE or not. We will then test whether existing clinical prediction rules can identify PE in pregnancy, and whether a new or improved rule works better in pregnancy.
This study is currently in the recruitment phase.
Study staff:
Di PEP
NHS National Institute for Health Research
UKOSS
UK Obstetric Surveillance System
Guy's and St Thomas' NHS
NHS Foundation Trust

Acknowledgements

- Beverley Hunt
- Catherine Nelson Piercy
- Druba Dasgupta
- Thrombosis UK

Previous VTE

- Women with previous VTE (except those with a single previous VTE related to major surgery and no other risk factors) should be offered thromboprophylaxis with LMWH throughout the antenatal period. [*New 2015*] [C]

- Women with VTE associated with either antithrombin deficiency or APS or with recurrent VTE (who will often be on long-term oral anticoagulation) should be offered thromboprophylaxis with higher dose LMWH

Previous VTE

•In women in whom the original VTE was provoked by major surgery from which they have recovered and who have no other risk factors, thromboprophylaxis with LMWH can be withheld antenatally until 28 weeks provided no additional risk factors are present (in which case they should be offered LMWH). They require close surveillance for the development of other risk factors [D]

Testing for thrombophilia in women with prior VTE

- Women with a family history of VTE and either antithrombin deficiency or where the specific thrombophilia has not been detected should be tested for antithrombin deficiency. [*New 2015*] . [✔]

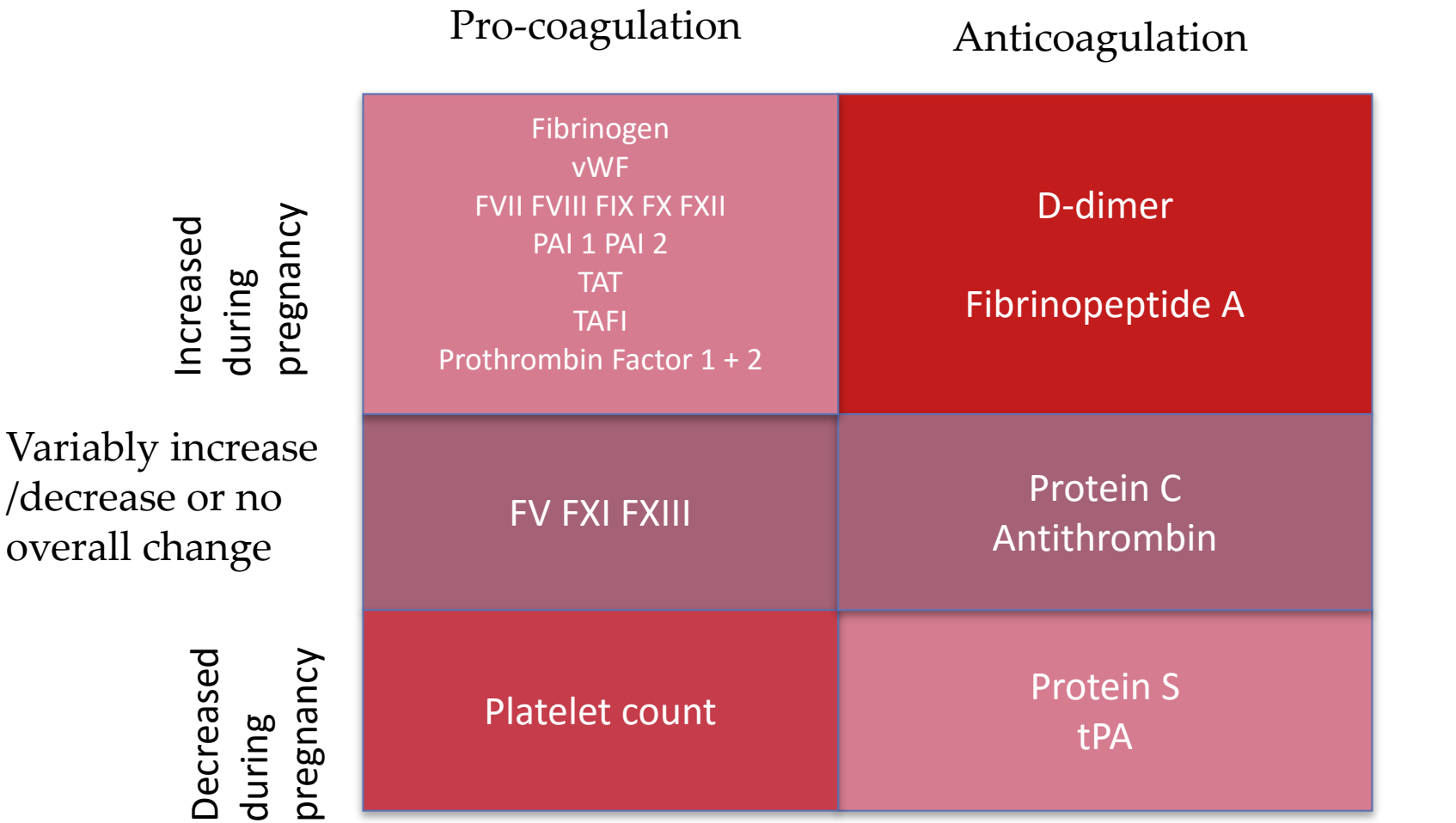
- Women with an unprovoked VTE should be tested for the presence of antiphospholipid antibodies. . [✔]

Asymptomatic thrombophilia

- Heterozygosity for factor V Leiden or prothrombin gene mutation or antiphospholipid antibodies are considered as risk factors for thrombosis in asymptomatic women. In the presence of three other risk factors such women may be considered for antenatal thromboprophylaxis, if there are two other risk factors thromboprophylaxis should be considered from 28 weeks and if there is one other risk factor postnatal thromboprophylaxis for 10 days should be considered.

- Women with no personal history or risk factors

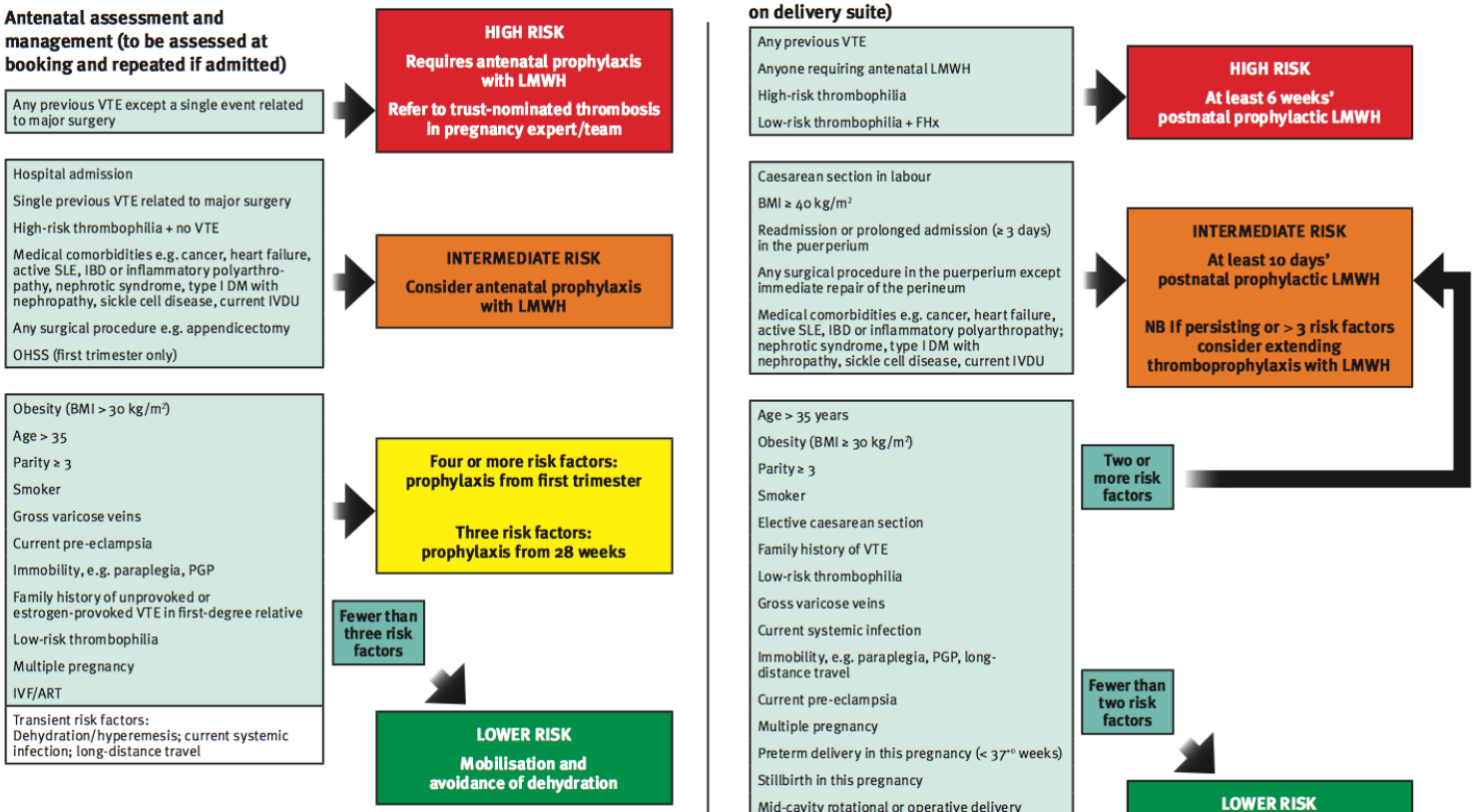
Haematological changes in pregnancy



Adapted from British Journal Anaesthesiology 2012

RCOG risk assessment

Appendix I: Obstetric thromboprophylaxis risk assessment and management



APL = antiphospholipid antibodies (lupus anticoagulant, anticardiolipin antibodies, β_2-glycoprotein 1 antibodies); ART = assisted reproductive technology; BMI based on booking weight; DM = diabetes mellitus; FHx = family history; gross varicose veins = symptomatic, above knee or associated with phlebitis/oedema/skin changes; high-risk thrombophilia = antithrombin deficiency, protein C or S deficiency, compound or homozygous for low-risk thrombophilias; IBD = inflammatory bowel disease; immobility = ≥ 3 days; IVDU = intravenous drug user; IVF = in vitro fertilisation; LMWH = low-molecular-weight heparin; long-distance travel = > 4 hours; low-risk thrombophilia = heterozygous for factor V Leiden or prothrombin G20210A mutations; OHSS = ovarian hyperstimulation syndrome; PGP = pelvic girdle pain with reduced mobility; PPH = postpartum haemorrhage; thrombophilia = inherited or acquired; VTE = venous thromboembolism.

Antenatal and postnatal prophylactic dose of LMWH

Weight < 50 kg = 20 mg enoxaparin/2500 units dalteparin/3500 units tinzaparin daily
Weight 50–90 kg = 40 mg enoxaparin/5000 units dalteparin/4500 units tinzaparin daily
Weight 91–130 kg = 60 mg enoxaparin/7500 units dalteparin/7000 units tinzaparin daily
Weight 131–170 kg = 80 mg enoxaparin/10 000 units dalteparin/9000 units tinzaparin daily
Weight > 170 kg = 0.6 mg/kg/day enoxaparin/ 75 u/kg/day dalteparin/ 75 u/kg/day tinzaparin

Appendix IV: Summary of guideline for thromboprophylaxis in women with previous VTE and/or thrombophilia (also see Appendix I)

Very high risk	Previous VTE on long-term oral anticoagulant therapy	Recommend antenatal high-dose LMWH and at least 6 weeks' postnatal LMWH or until switched back to oral anticoagulant therapy
	Antithrombin deficiency Antiphospholipid syndrome with previous VTE	*These women require specialist management by experts in haemostasis and pregnancy*
High risk	Any previous VTE (except a single VTE related to major surgery)	Recommend antenatal and 6 weeks' postnatal prophylactic LMWH
Intermediate risk	Asymptomatic high-risk thrombophilia homozygous factor V Leiden/compound heterozygote Protein C or S deficiency	Refer to local expert Consider antenatal LMWH Recommend postnatal prophylactic LMWH for 6 weeks
	Single previous VTE associated with major surgery without thrombophilia, family history or other risk factors	Consider antenatal LMWH (but not routinely recommended) Recommend LMWH from 28 weeks of gestation and 6 weeks' postnatal prophylactic LMWH
Low risk	Asymptomatic low-risk thrombophilia (prothrombin gene mutation or factor V Leiden)	Consider as a risk factor and score appropriately (see Appendix III) Recommend 10 days' if other risk factor postpartum (or 6 weeks' if significant family history) postnatal prophylactic LMWH

Maternal death rate 2003-12

(Three year rolling averages)