

Anticoagulant treatment during pregnancy in women with heart diseases

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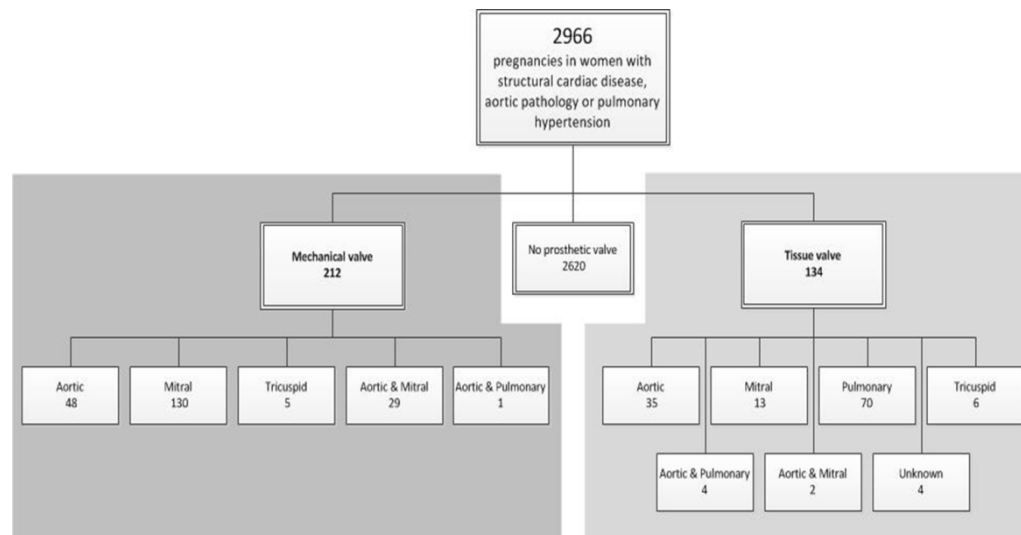
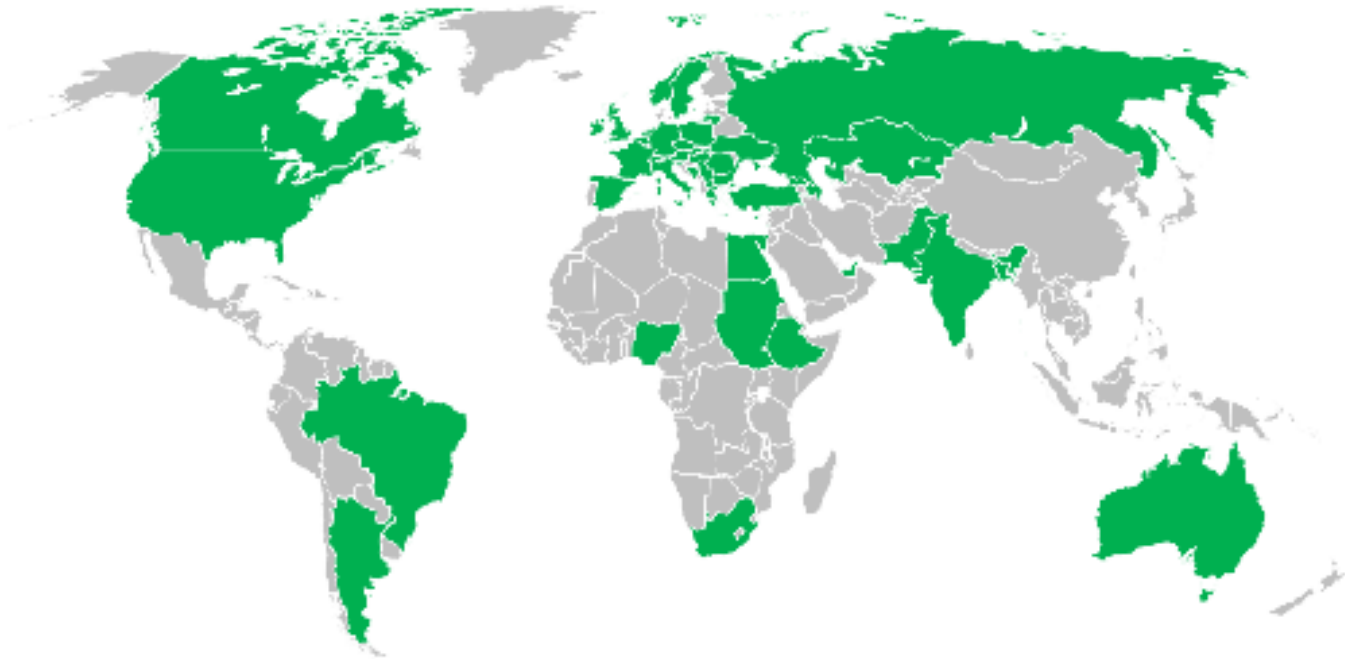
Indications for Anticoaguation in Pregnant Women with Heart Disease

- Mechanical heart valves
- Fontan circulation
- Atrial Fibrillation
- Dilated cardiomyopathy / Peripartum cardiomyopathy
- Pulmonary hypertension



ROPAC Registry

48 countries, 132 centers, 2966 pregnancies

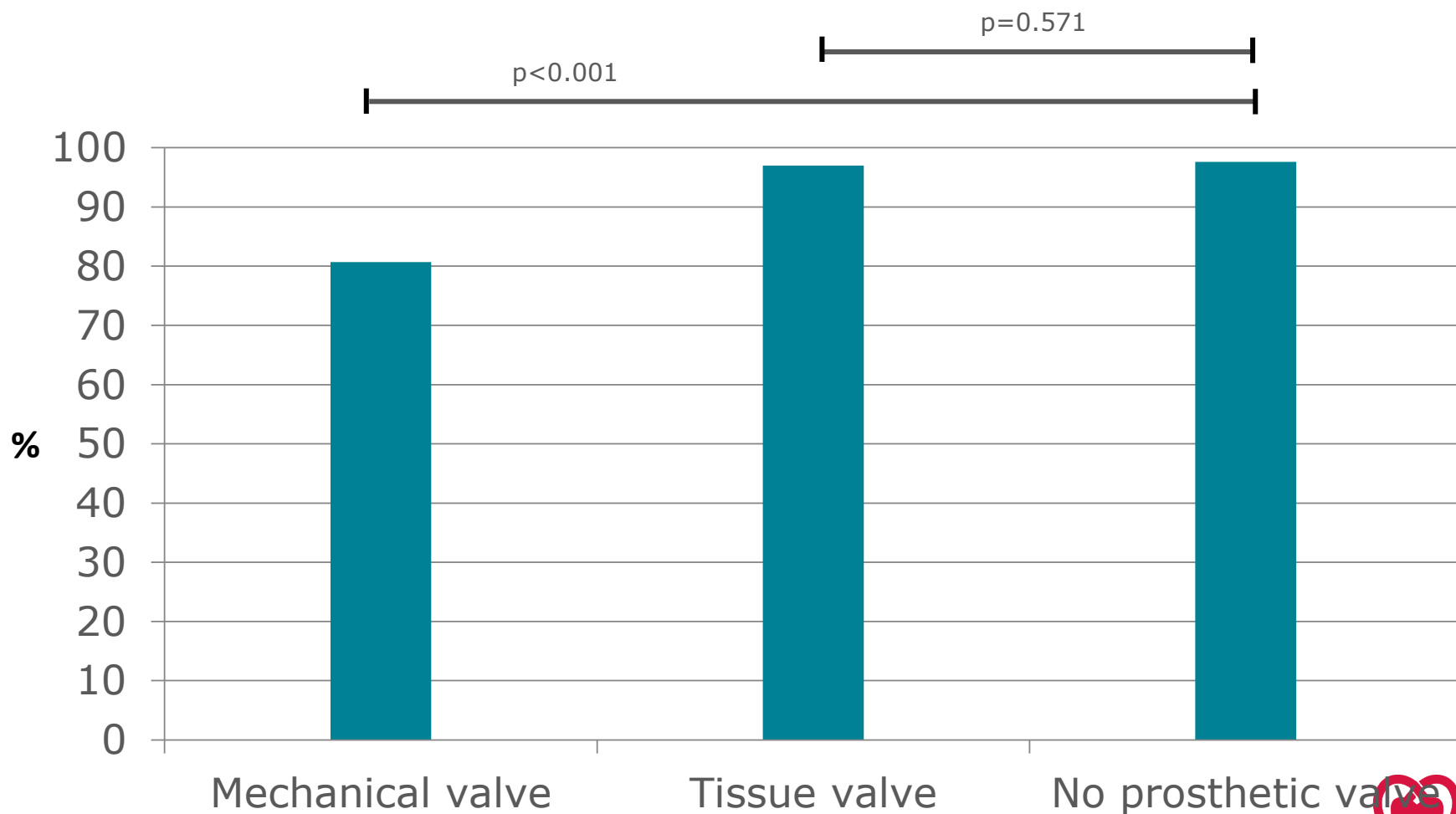


Results *Complications*

	Mechanical valve 212	Cardiac patients No prosthesis 2620
Maternal mortality	1.4%	0.2%*
Thrombotic event	6.1%	0.4%*
Haemorrhagic event	23%	5%*
Miscarriage <24 wks	15.6%	1.7%*
Fetal mortal >24 wks	2.8%	0.6%*

* $p < 0.05$

Results *Live births*



Case Study 1: Morbidity

A woman who spoke very little English had a mechanical mitral valve replacement as a child. During pregnancy she was prescribed once daily LMWH and there was no monitoring of Anti Xa levels. She did not see an obstetrician until mid pregnancy, and did not see a consultant (obstetrician or cardiologist) or have an echo until the third trimester. LMWH was stopped prior to induction. She had a normal delivery, was discharged and asked to make her own anticoagulant clinic appointment. Two weeks later she was had a mitral valve thrombosis which was treated successfully with thrombolysis, but two weeks later she had a thromboembolic stroke.

* A morbidity case

Case Study 2: Mortality

A woman who had previously undergone prosthetic valve replacement became unexpectedly pregnant and requested TOP. She was changed to LMWH but initially the dose was inappropriately low, and only once daily. The day before TOP she was breathless and coughing pink frothy sputum. She was tachycardic, tachypnoeic and hypoxic. In ICU she was ventilated and treated for a chest infection. An echo was thought to show right heart strain. The possibility of valve thrombosis was not considered. Four days later the echo was reviewed and a thrombosed mitral valve diagnosed. The woman died 2 days later.

Anticoagulation in Pregnancy: Warfarin vs Heparin



Risks to Mother

Risks to Fetus

Anticoagulation for Mechanical Valves

Warfarin

vs

Heparin

Effective maternal anticoagulant

Less effective maternal anticoagulant

BUT

BUT

Crosses placenta

Doesn't cross placenta

Fetal effects

Neonatal haemorrhage

Less neonatal haemorrhage

Maternal haemorrhage

Less maternal haemorrhage

Low Molecular Weight Heparin

Warfarin Embryodystrophy

Abnormal bone & cartilage formation

Nasal bone hypoplasia

Nose flattened, depressed or ruptured

Hypertelorism

Brachydactyly

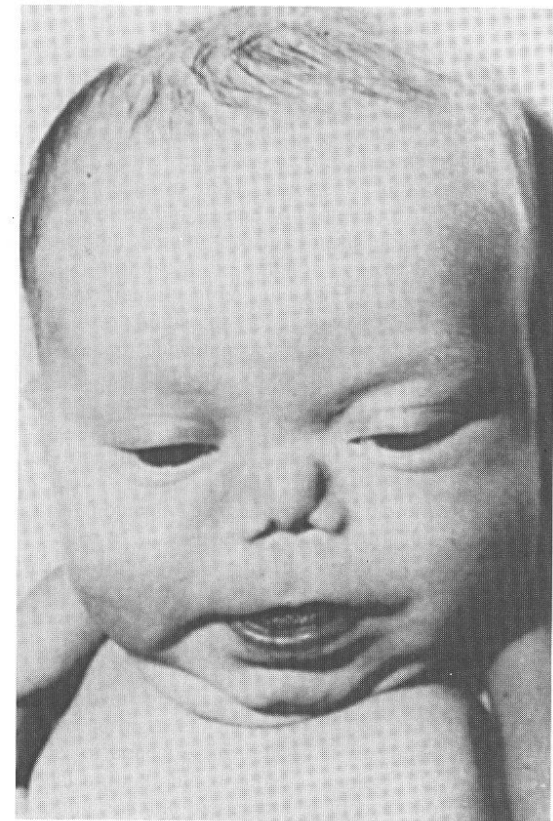
Hypoplasia of terminal phalanges

Skull abnormalities

Scoliosis

Epiphyseal stippling on XR

Cognitive dysfunction (IQ<80)



Fetal Warfarin Syndrome: infant with hypoplastic nose, flat face and low nasal bridge as well as altered calcification (Smith 1982).

Greatest risk if exposure between 6-12/40

Shaul et al Am J Obstet Gynecol '77
Bonow et al Circ '98,

Other Fetal Anomalies Associated with Warfarin Use in Pregnancy

- ♥ Congenital heart disease (truncus arteriosus, VSD)
- ♥ Intrauterine growth restriction
- ♥ Occipital meningocele Oakley'97
- ♥ **Fetal neurological disease**

Due to cerebral & intraventricular haemorrhage

Risk *throughout* pregnancy

- Optic atrophy, microphthalmia, blindness, cataracts
- Deafness,
- Seizures, spasticity, microcephaly

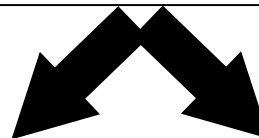
Dose-Dependent Fetal Complications of Warfarin in Pregnant Women With Mechanical Heart Valves

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71 pregnancies with mechanical valve
Warfarin until 48h before elective CS at 37/40 (target INR 2.25-4)

Pregnancy loss /stillbirth	28 (39%)
Embryopathy	4 (5.5%)
Maternal death,	0
Thromboembolism,	
Haemorrhage	



Warfarin	>5mg n=33	≤5mg n=38
Poor outcome (Embryopathy	27 (82%) 3	3 (9%) 1)



Mechanical Valves in Pregnancy

Not all prosthetic valves are the same



Aortic position
Large

Mitral position
Small

Increasing thrombogenicity

Warfarin vs UFH for Mechanical Valves

Systematic Literature Review

- 28 articles; 6 cohort studies, 22 case series
- 1966-1997; 976 women, 1234 pregnancies
- *50% caged ball vs 7% bileaflet*
- *2/3 mitral*

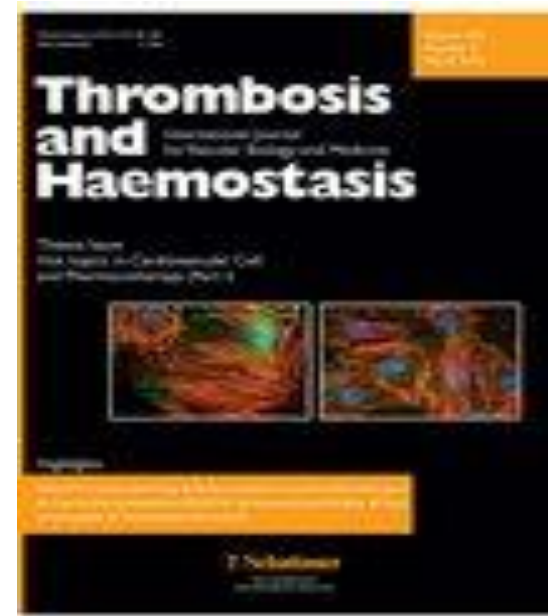
Warfarin vs UFH for Mechanical Valve

	Warfarin n=792	Heparin, Warfarin, Heparin n=230	Heparin (low/full dose) n=21
Fetal loss	34%	16%	34%
Embryopathy	6.4%	0	0
Thromboembolism	4%	9%	33%
Maternal mortality	1.8%	4.2%	15%

LMWH in Pregnancy for Prophylaxis of Thromboembolism in Mechanical Valves

Systematic review, 1989-2003

- 67 pregnancies in 61 women
 - 32 MVR
 - 8 AVR
 - 3 both
 - 18 unspecified
- 12 first trimester
- 55 throughout



*Oran, Lee-Parritz & Ansell.
2004; 94: 747-751.*

LMWH in Pregnancy for Prophylaxis of Thromboembolism in Mechanical Valves

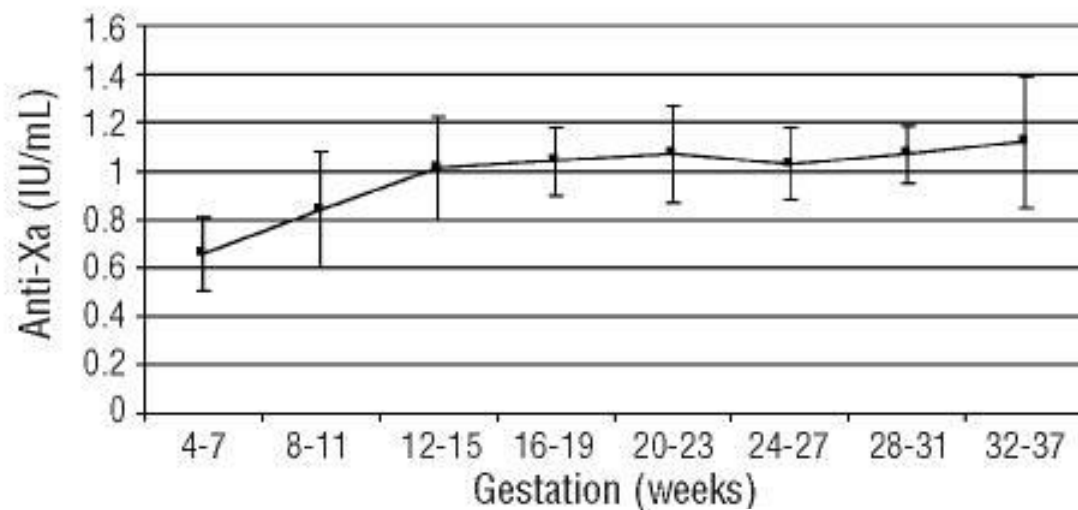
- Maternal mortality 1/67 (1.49%)
- Intracranial haemorrhage 3/12
- Live birth = 86.5%
 - Miscarriage in 5/67 (7.5%)
 - Stillbirth in 1/67
 - 2nd trimester loss in 2/67
 - 1 hydrocephalus on warfarin
 - 1 after ovarian surgery on IV unfractionated heparin

*Oran, Lee-Parritz & Ansell.
2004; 94: 747-751.*

LMWH vs Warfarin

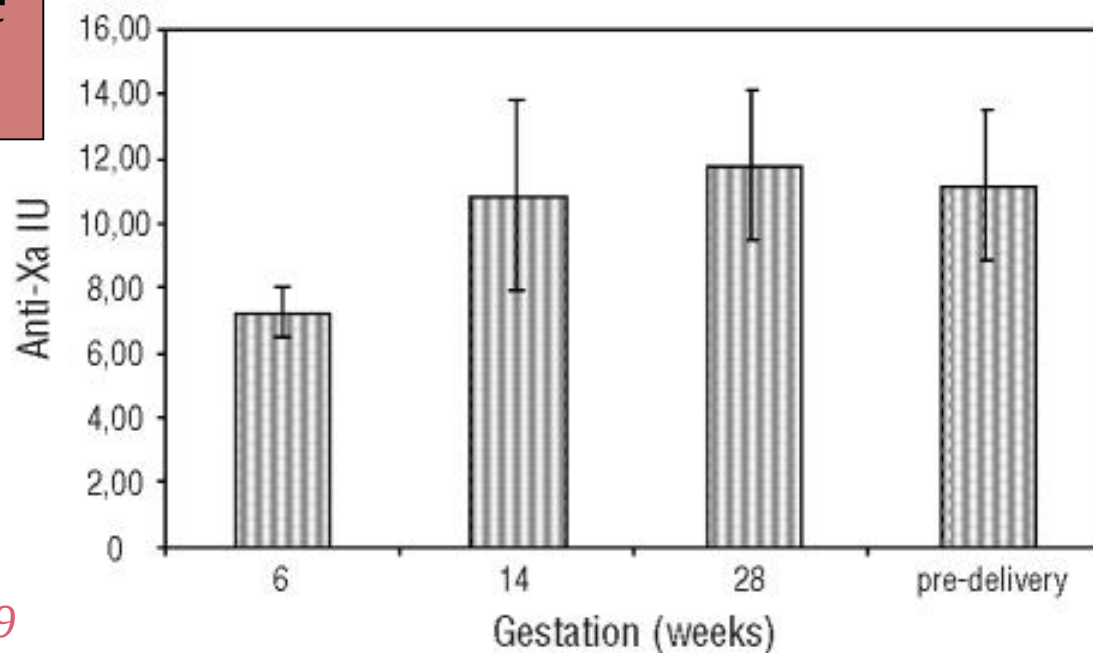
- Aortic valve
 - Newer valve
 - Carbomedics
 - Sinus rhythm
 - Warfarin dose $> 5\text{mg}$
 - Likely compliance with 2 injections / day
 - Give adjunctive aspirin
- Mitral valve
 - Older (smaller) valve
 - Bjork-Shiley
 - AF/ large LA
 - Warfarin dose $< 5\text{mg}$
 - > 1 mechanical valve
 - Previous CVA / embolus

Mean anti-Xa levels ($\pm$ SD)



Mean increase in dose
of LMWH of 54%

Mean number of anti-Xa units administered 12 hourly during all pregnancies ($\pm$ SD)



Delivery



- No delivery under vit K blockers
 - Fetal risk of cerebral bleeding

(Sareli et al. Am J Cardiol 1989;63:1462-5)
 - Prolonged anticoagulation in the fetus
- Substitution by heparin at 36th week
 - Heparin discontinued at the onset of labour and resumed 4-6 h after delivery
- Cesarean section
 - ↓ risk of intracerebral fetal haemorrhage
 - ↑ maternal risk of bleeding and thromboembolism
- Vaginal delivery
 - Consider risk of peridural analgesia



ESC Guidelines on the management of cardiovascular diseases during pregnancy

The Task Force on the Management of Cardiovascular Diseases during Pregnancy of the European Society of Cardiology (ESC)

Endorsed by the European Society of Gynecology (ESG), the Association for European Paediatric Cardiology (AEPC), and the German Society for Gender Medicine (DGesGM)

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Recommendations for the management of valvular heart disease

Recommendations	Class	Level
Continuation of OACs should be considered during the first trimester if the warfarin dose required for therapeutic anticoagulation is < 5 mg/day (or phenprocoumon < 3 mg/day or acenocoumarol < 2 mg/day), after patient information and consent.	IIa	C
Discontinuation of OAC between weeks 6 and 12 and replacement by adjusted-dose UFH (a PTT $\geq 2 \times$ control; in high risk patients applied as intravenous infusion) or LMWH twice daily, (with dose adjustment according to weight and target anti-Xa level 4-6 hours post-dose 0.8-1.2 U/mL) should be considered in patients with a warfarin dose required of more than 5 mg/day (or phenprocoumon > 3 mg/day or acenocoumarol > 2 mg/day).	IIa	C
LMWH should be avoided, unless anti-Xa levels are monitored.	III	C

Recommendations for the management of valvular heart disease

Recommendations	Class	Level
OAC should be discontinued and dose-adjusted UFH (a PTT $\geq 2 \times$ control) or adjusted-dose LMWH (target anti-Xa level 4-6 hours post-dose 0.8-1.2 U/mL) started at the 36 th week of gestation.	I	C
In pregnant women managed with LMWH, the 4-6 hours post-dose anti-Xa level should be assessed weekly.	I	C
LMWH should be replaced by intravenous UFH at least 36 hours before planned delivery. UFH should be continued until 4-6 hours before planned delivery and restarted 4-6 hours after delivery if there are no bleeding complications.	I	C

So... what are the anticoagulation options in pregnant women with mechanical valves?

- Any strategy carries risks
- Women should participate in the choice of anticoagulation
- Women should be fully informed of risks and benefits of all options
- Decision should be individualized and ideally made pre pregnancy
- Care should be multidisciplinary and centralized



Case Study 3: Optimal Management

A woman who had a metallic prosthetic aortic valve and root replacement had a planned pregnancy, following pre-pregnancy counselling. During the pregnancy she had multidisciplinary care, and regular review by senior clinicians, with intensive monitoring of her anticoagulation. Her heart valve function deteriorated. A care plan including obstetric, cardiac, anaesthetic and haematological elements was generated. She underwent successful elective LSCS at term with an excellent outcome.

