

**Pregnancy outcomes in women with mechanical prosthetic heart valves: a prospective descriptive population based study using the United Kingdom Obstetric Surveillance System (UKOSS) data collection system**

\*Dr Sarah Vause<sup>1,2</sup>

Professor Bernard Clarke<sup>3,4</sup>

Dr Clare L Tower<sup>1,2</sup>

Professor Charles RM Hay<sup>5,6</sup>

Professor Marian Knight (on behalf of UKOSS)<sup>7</sup>

1. Obstetric Directorate, St Mary's Hospital, Central Manchester University Hospitals NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester M13 9WL

2. Institute of Human Development, Faculty of Medical and Human Sciences, University of Manchester

3. Manchester Heart Centre, Manchester Royal Infirmary, Central Manchester University Hospitals NHS Foundation Trust, Oxford Road, Manchester M13 9WL

4. Institute of Cardiovascular Sciences, Manchester Academic Health Science Centre, University of Manchester

5. Department of Haematology, Manchester Royal Infirmary, Central Manchester University Hospitals NHS Foundation Trust, Oxford Road, Manchester M13 9WL

24

25       6. Institute of Cancer Sciences, Manchester Academic Health Science Centre, University of  
26       Manchester

27

28       7. National Perinatal Epidemiology Unit, Old Road Campus, University of Oxford, Oxford  
29       OX3 7LF

30

31   **\*Corresponding author:**

32   Dr Sarah Vause, Consultant in Fetal and Maternal Medicine, St Mary's Hospital, Oxford Road,  
33   Manchester M13 9WL

34   Tel: 0161 276 6426

35   email: sarah.vause@cmft.nhs.uk

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38

39    **Abstract**

40    **Objective**

41    To describe the incidence of mechanical prosthetic heart valves (MPHV) in pregnancy in the  
42    UK; rates of maternal and fetal complications in this group of women, and whether these vary  
43    with the anticoagulation used during pregnancy.

44    **Design**

45    Prospective descriptive population based study

46    **Setting**

47    All consultant-led maternity units in the UK

48    **Population**

49    All women with a MPHV who were pregnant between 1<sup>st</sup> February 2013 and 31<sup>st</sup> January 2015

50    **Methods**

51    Collection and analysis of anonymous data relating to pregnancy management and outcome,  
52    using the UKOSS notification and data collection system

53    **Main Outcome Measures**

54    Maternal death, serious maternal morbidity, poor fetal outcome

55    **Results**

56    Data were obtained on 58 women giving an estimated incidence of 3.7 (95% CI 2.7-4.7) per  
57    100,000 maternities. There were 5 maternal deaths (9%); a further 24 (41%) suffered serious  
58    maternal morbidity. There was a poor fetal outcome from 26 (47%) pregnancies. Only 16 (28%)  
59    women had a good maternal and good fetal outcome. Low Molecular Weight Heparin (LMWH)

was used throughout pregnancy by 71% of women. Of these 83% required rapid dose escalation in the first trimester. Monitoring regimes lacked consistency.

## **Conclusions**

This study has estimated the incidence of MPHVs in pregnant women in the UK. It includes the largest cohort managed with LMWH throughout pregnancy reported to date. It demonstrates a high rate of maternal death, serious maternal and fetal morbidity.

Women with MPHVs, and their clinicians need to appreciate the significant maternal and fetal risks involved in pregnancy. Care should be concentrated in specialist centres.

## **Keywords**

Pregnancy; mechanical prosthetic heart valve; anticoagulation; maternal outcome; fetal outcome

## **Tweetable abstract**

High rates of poor maternal and fetal outcomes in pregnant women with mechanical prosthetic heart valves

## Introduction

Women with mechanical prosthetic heart valves (MPHV) require lifelong anticoagulation to prevent valve thrombosis. Pregnancy is thrombogenic, and thus represents a time of significant clinical risk. It is believed that increasing numbers of women with MPHVs are embarking on pregnancy<sup>1</sup>, but optimal clinical management is hampered by a lack of good quality data on maternal mortality and rates of complications.

Three anticoagulant regimes are commonly used in pregnancy: warfarin throughout; low molecular weight heparin (LMWH) throughout; or LMWH in the first trimester, then warfarin until the mid-third trimester, converting back to LMWH or unfractionated heparin prior to delivery. Warfarin is thought to have the lowest risk of maternal complications<sup>2</sup> but is associated with higher rates of fetal complications and demise<sup>3,4</sup>. LMWH is safe for the fetus, but doubts have been expressed about its efficacy in preventing maternal complications<sup>5,6</sup>. European Society for Cardiology (ESC) guidelines have called for more research to identify the best treatment for pregnant women<sup>7</sup>. Various expert groups have suggested that women themselves should make an 'informed choice' about which regime to use but currently there is very little evidence to aid them in this choice.

The aims of this study were

1. to ascertain how many women with prosthetic valves become pregnant each year in the UK
2. to report the incidence of fetal and maternal complications in women with MPHVs in pregnancy
3. to describe the incidence of complications associated with the different anticoagulation regimes used in contemporary UK practice.

## 98 **Methods**

### 99 *Research Design*

100 This prospective descriptive population based study used the United Kingdom Obstetric  
101 Surveillance System (UKOSS) data collection system to identify all women in the UK with  
102 MPHVs in pregnancy<sup>8</sup>.

### 103 *Case definition*

104 A case was defined as any woman in the UK, with an artificial mechanical prosthetic heart  
105 valve, who became pregnant in a two year period between 1<sup>st</sup> February 2013 and 31<sup>st</sup> January  
106 2015, irrespective of the pregnancy outcome.

107 This included any woman in whom one or more heart valves had been replaced with an artificial  
108 mechanical prosthetic heart valve. Women with a bioprosthetic valve or homograft were  
109 excluded.

### 110 *Data collection*

111 Cases were identified from a monthly mailing of UKOSS notification cards to a nominated  
112 reporting clinician in each of the 210 UK hospitals with a consultant-led maternity unit. They  
113 were asked to return all cards, including those with 'nil to report'. When a card was returned  
114 indicating that there had been a pregnancy in a woman with a prosthetic valve, the reporting  
115 clinician was sent a data collection form. The form gathered detailed information about the  
116 woman including the type and position of valve, anticoagulant regime and maternal and fetal  
117 outcomes. Cases were allocated UKOSS identification numbers and all data were anonymous.  
118 Once received, duplicate cases were excluded by comparison of key clinical information. The  
119 data were double entered into a customised database by two individuals and the data compared  
120 to minimise data entry errors. Case details were reviewed against the case definition and all

cases that did not meet the inclusion criteria were excluded. Reminders were sent if forms were not returned or were incomplete. At the close of the data collection period, contact was made with specialist centres to check case ascertainment was complete.

#### *Statistical analysis*

Since women with MPHVs would not be cared for in any setting other than a consultant led maternity unit, data on cases were obtained from these units. The total number of maternities in the UK over the two years of the study was used as the denominator when calculating the incidence. This study therefore covers the entire birth cohort within the UK. Incidence was calculated with 95% confidence intervals.

Maternal and neonatal outcomes were compared in pre-specified subgroups according to the anticoagulant and regime used. Anticoagulant regimes were categorised as 'Warfarin throughout'; 'LMWH throughout' and 'First trimester LMWH with subsequent warfarin' or 'Other'. Reporting clinicians were asked to select the regime which best described the woman's anticoagulation management, and data were also collected on the anticoagulant being used at 10 and 20 weeks gestation.

A poor maternal outcome was defined as maternal death or serious morbidity (admission to intensive care for more than one day; valve thrombosis or valve dysfunction resulting in heart failure; cerebrovascular accident (CVA); or bleeding complications requiring transfusion or return to theatre (primary postpartum haemorrhage, secondary postpartum haemorrhage, intra-abdominal bleeding, vaginal haematoma, wound haematoma)). A poor fetal outcome was defined as any pregnancy loss (miscarriage or termination of pregnancy); stillbirth; neonatal death; fetal abnormality; Apgar score of <7 at 5 minutes; or admission to the neonatal unit.

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147 Maternal death was defined as death during pregnancy or up to 42 days after delivery.

148 Miscarriage was the loss of pregnancy up to 24 weeks gestation. Stillbirth was a baby born  
149 following an intrauterine fetal death after 24 weeks 0 days gestation. Preterm birth was defined  
150 as delivery before 37 weeks gestation.

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#### 152 *Ethics committee approval*

153 The UKOSS general methodology (04/MRE02/45) was approved by the London Multicentre  
154 Research Ethics Committee. This study was approved by the NRES Committee Yorkshire &  
155 Humber - Sheffield (study reference 13/YH/0048 - 7<sup>th</sup> February 2013).

156

## 157 **Results**

158 All 210 hospitals with consultant-led maternity units in the UK participated in the study.

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160 Eighty-three cases were reported, and 75 forms returned. There were 8 duplicates and 9  
161 women did not meet the case definition. No additional cases were identified through sources  
162 other than UKOSS. There were thus 58 women with confirmed MPHVs in pregnancy, in an  
163 estimated 1 555 000 maternities, giving an overall estimated incidence of 3.7 (95% CI 2.7-4.7)  
164 per 100,000 maternities. Table 1 shows the demographic characteristics of the women.

165 One of the 58 women in the study had her prosthetic valve implanted during pregnancy (second  
166 trimester). Of the 57 women who had MPHVs prior to pregnancy, 33 (58%) presented before 7  
167 weeks gestation. Five women miscarried (3 in the first trimester and 2 second trimester), 4  
168 women terminated their pregnancies and two women died undelivered. The number of women



who had presented for care and had ongoing pregnancies therefore changes across gestation with 33 women before 7 weeks gestation; 43 women at 10 weeks; 47 women at 20 weeks and 47 women reaching the third trimester (>24 weeks).

Of the 57 women who had a prosthetic valve in situ prior to becoming pregnant, 13 (23%) had not been reviewed by a cardiologist in the year preceding their pregnancy (one woman had a prosthetic valve inserted during pregnancy). Eleven women (19%) were not referred either to tertiary care or to a specialist obstetric-cardiology service during their pregnancy.

Twenty nine women (51%) had pre-pregnancy counselling; 28 women (49%) either did not, or there was no evidence of it recorded. One woman underwent a valve replacement at 20 weeks gestation following an unexpected aortic dissection, thus pre-pregnancy counselling was impossible. The women who had received pre-pregnancy counselling did not present earlier in gestation (median 6 weeks, range 4-16 weeks), than those who had not (median 7 weeks, range 4-24 weeks) (Wilcoxon  $p=0.29$ ).

### *Haematological Management*

Of the 33 women who presented at less than 7 weeks, 3 (9%) were already using LMWH pre-pregnancy, and 21 (64%) converted to LMWH prior to 7 weeks gestation; 2 of these women (6%) used warfarin throughout pregnancy; one (3%) elected to have a termination and therefore did not convert to LMWH. In 4 women (12%) the timing of conversion to LMWH was not known and in 2 women (6%) it occurred between 7 and 8 weeks gestation.

The most common anticoagulant regime was LMWH throughout pregnancy which 71% of women used (Table 2).

191 At 10 weeks gestation 25 of the 30 (83%) women using LMWH required a dose in excess of that  
192 recommended in the British National Formulary (BNF)<sup>9</sup>. At 20 weeks gestation 25 of the 28  
193 women (89%) required a higher dose.

194 Data on the monitoring regime were provided for 32 women. There was variation in the  
195 frequency of monitoring anti Xa levels, varying from not at all, to weekly. Post dose anti Xa  
196 levels were taken between 0 and 5 hours (median 3 hours). In 15 of 32 (47%) women only post  
197 dose anti Xa levels were checked (not pre dose). The incidence of maternal complications was  
198 similar in the women who only had post dose anti Xa levels checked (47%) compared to those  
199 who had both pre and post dose levels (52%).

200 There was wide variation in target ranges documented, but the median target ranges stated  
201 were pre-dose 0.3-1U/ml and post dose 0.9-1.2U/ml. For 11 women, the reported target ranges  
202 were inappropriate for pregnancy<sup>7</sup> with the lower end of the pre-dose target range being given  
203 as 'detectable' for 3 women, and the upper end of the post-dose target range being given as  
204 2.5U/ml for 8 women.

205 The median number of times anti Xa levels were monitored was 10 (range 0-75). In the 40  
206 women where it could be assessed, doses of LMWH were changed after monitoring on 126 of  
207 591 occasions (21% of the time). Women who experienced thrombotic complications (n=8),  
208 were more likely to be using an inappropriate dose and need a dose change (50% of the time)  
209 than those who did not have thrombotic complications (17% of the time) (Chi squared  $p < 0.001$ ).

210 There was a non significant trend for women with thrombotic complications to have less  
211 frequent monitoring (median 8 compared to median 10 in women without thrombotic  
212 complications).

213 Of the 24 women who remained on the same preparation of LMWH throughout pregnancy only  
214 7 did not require a dose increase between 10 and 20 weeks gestation. 16 women required a 12-  
215 100% increase in dose. (Unable to assess one woman).

216 Poor compliance was reported for 11 women, 7 (64%) of whom had a poor maternal outcome.  
217 Of the 47 women with good compliance 22 (47%) had a poor maternal outcome (Chi squared  
218  $0.5 > p > 0.1$ ). The proportion of thrombotic complications was similar in women with poor  
219 reported compliance (50%), and no reported compliance problems (42%).

220 Of the 47 women who reached the third trimester, information was available about the timing of  
221 reintroduction of warfarin postnatally for 39. The median time for recommencement of warfarin  
222 was 2 days postnatally (range 0-35). For women with bleeding complications the median was 5  
223 days (n=16, range 1-35), and for those who did not experience bleeding complications 2 days  
224 (n=23, range 0-8).

#### 225 *Obstetric management*

226 There were 47 women who reached the third trimester of pregnancy (>24 weeks 0 days  
227 gestation). One was lost to follow up and no data are available about the management of  
228 delivery or neonatal outcome.

229 There was a care plan for delivery in the notes of 40 (85%) women, and 39 of these included  
230 the management of anticoagulation.

231 Twenty one women (45%) had a vaginal delivery, with 25 (53%) having a Lower Segment  
232 Caesarean Section (LSCS) (One not known) (Table 3). Only one LSCS was performed in  
233 labour, the others being done electively. There was no difference in the proportion of nulliparous  
234 (45%) or parous women (44%) who delivered vaginally.

Of the 25 LSCS, 5 were performed for fetal compromise, 13 for maternal compromise, 3 in view of previous LSCS, 1 for maternal request, 1 for failed induction, 1 for failure to progress in labour and 1 indication not known.

#### *Maternal outcomes*

There were 5 deaths (9%) among this group of 58 women with a MPHV in pregnancy. Their ages ranged from 24-38 years; 2 were nulliparous; 3 were White British and 2 African. Their prosthetic valves had been implanted between 1-22 years before the pregnancy: 2 were in the aortic position and 3 in the mitral position. Four women had pre-pregnancy counselling. All women were using warfarin prior to pregnancy, but all changed to LMWH in pregnancy. Two women with valve thrombosis died in the first half of pregnancy; 2 women died immediately post-pregnancy from valve dysfunction / cardiac failure; one woman died from a cerebrovascular accident (CVA).

In addition to the women who died, 24 women (41%) had serious maternal morbidity (Table 3). Postpartum bleeding complications which necessitated return to theatre or transfusion were experienced by 17 (29%) women. Of the 25 women delivered by LSCS, 10 (40%) needed to return to theatre due to bleeding complications; 7 (33%) of the 21 women who delivered vaginally had haemorrhagic complications ( $p>0.5$  Chi squared).

Of the 28 women with a prosthetic mitral / systemic atrioventricular valve alone, 16 (57%) had serious maternal morbidity or mortality; of the 26 women with a prosthetic aortic valve alone the figure was 10 (39%), ( $0.5>p>0.1$  Chi squared). Of the 4 women with both a prosthetic mitral and aortic valve 3 (75%) had serious maternal morbidity or mortality. In the surviving women, all 5 valve thromboses occurred in women with prosthetic mitral valves; of the 4 women who had CVAs, 3 had prosthetic aortic valves and one had a prosthetic mitral valve.

The proportion who smoked was 22%, almost double that of the UK pregnant population<sup>10</sup>.

Smoking status was not related to poor maternal outcome ( $0.5 > p > 0.1$  Chi squared).

### *Neonatal outcome*

There was a poor fetal outcome in 27 (47%, 95% CI 34-59%) of the 58 pregnancies, and in 16 (35%, 95% CI 21-49) of those reaching the third trimester (Table 3). If terminations of pregnancy were excluded from the analysis 43% of pregnancies had a poor fetal outcome.

Of the eleven babies born before 37 weeks gestation, 3 were due to spontaneous preterm labour, the other 8 being delivered electively (5 due to fetal compromise and 3 for maternal reasons).

There were 2 fetal anomalies; 1 fetal warfarin syndrome in a woman who used warfarin throughout her pregnancy and one inherited genetic condition compatible with long term survival (unrelated to cardiac condition or anticoagulation). In addition, two women had red cell antibodies rendering the fetus at risk of alloimmunisation.

### *Maternal and fetal outcomes associated with the different anticoagulation regimes*

Overall only 16 women (28%) had good maternal and fetal outcomes. In women using LMWH throughout pregnancy only 8 of the 41 women (20%) had good maternal and fetal outcomes, whereas in the women using LMWH in the first trimester and warfarin subsequently this was the case for 5 of the 9 women (56%) (Table 4).

## **Discussion**

### ***Main findings***

This study estimated the incidence of MPHVs to be 3.7 per 100,000 maternities in the UK. It includes the largest cohort of women with MPHVs managed with LMWH throughout pregnancy reported to date. It demonstrates a high rate of maternal death, serious maternal and fetal morbidity.

### ***Strengths and Limitations***

The data collection methodology used provides an unbiased cohort and is the only prospective, population based (national) study of pregnancies with MPHVs in situ. Other published cohorts relate to self-selecting centres<sup>5,11,12,13,14,15</sup> particular treatment regimes<sup>12,15,16</sup>, valves in a particular position<sup>15,17</sup>; or are retrospective population studies of birth registry data<sup>1,18</sup>.

The limitations of this study are that some data were incomplete as the care of many women was shared between different disciplines, frequently between different hospitals, and in 8 (10%) cases the form was not returned. As the study was prospective, the implication of the data collection process on involved centres' practices is unknown. To preserve anonymity of women some details could not be reported as the woman would be identifiable.

In this national study over a two year period, the number of women remained small, thus limiting the study power to detect as statistically significant, what might be clinically important differences between subgroups. This was particularly true when considering outcomes with different anticoagulant regimes. Small numbers also limited the ability to investigate confounders such as underlying cardiac diagnosis or functional status.

### ***Interpretation***

*Incidence of MPHVs in pregnancy in the UK (2013-2015)*

During the study period 3.7 per 100,000 maternities (95% CI 2.7-4.7 per 100,000) occurred in women with MPHVs, higher than in the only other study to estimate incidence<sup>18</sup> (1.8/100,000 maternities 95% CI 1.0-2.5 per 100,000 in New South Wales, Australia 2000-2011). This could represent differences in populations; an increase in the number of women with MPHVs embarking on pregnancy<sup>1</sup>; or better case ascertainment.

#### *Incidence of fetal and maternal complications in women with MPHVs in pregnancy*

There were high rates of maternal mortality (9%) and serious maternal morbidity (41%): 16% of women sustained valve thrombosis or dysfunction; 9% suffered CVA; 29% had obstetric haemorrhage. These figures are higher than those reported in a recent systematic review (maternal mortality 1.8%; obstetric haemorrhage 11.1%; thromboembolic event 13.9%)<sup>19</sup> or in the largest single series to date (ROPAC Registry) (maternal mortality 1.4%, thrombotic complications 6.1%, heart failure 7.5%, haemorrhagic complications 23.1%)<sup>20</sup>. Our study was a prospective national cohort study and therefore less likely to be subject to reporting bias. Alternatively, it could reflect a real increase in the rate of maternal complications with the anticoagulation regimes used. The majority of women in our study were using LMWH, whilst those in studies included in the systematic review<sup>19</sup> and the ROPAC registry<sup>20</sup> mainly used warfarin, either throughout, or during the second and third trimesters of pregnancy.

The rate of haemorrhagic complications (29%), was similar to that reported by Abildgaard (33%)<sup>16</sup>. In common with this study, the complications were predominantly due to secondary haemorrhage (wound haematoma, secondary postpartum haemorrhage and intraabdominal bleeding). Although secondary haemorrhage is a recognised postoperative complication occurring when warfarin is restarted<sup>21</sup>, in our study it did not appear to be due to early rewarfarinisation. The appropriate anticoagulation regime, in the immediate postpartum period when circulating volume is changing rapidly is still unknown.

There was a suggestion of worse maternal outcomes in women with a prosthetic mitral / systemic atrioventricular valve (57%), compared to an aortic valve (39%), although this was not statistically significant. Women with two MPHVs had the worst outcomes (75%). In this cohort, where valve thrombosis complicated pregnancy it only occurred in association with prosthetic mitral valves. The ROPAC registry also suggested more valve thromboses in the women with prosthetic mitral valves (mitral 4.4%, aortic 2.6%)<sup>20</sup>.

Few published series detail neonatal outcomes, yet this appears to be important to women and influences their choice of anticoagulation regime. This study demonstrates a high rate of fetal morbidity and mortality, with a poor fetal outcome in 47% of the cohort, and 35% of those reaching the third trimester, higher than other reported series<sup>18,20</sup>.

#### *Incidence of fetal and maternal complications with the different anticoagulation regimes used*

This study has described outcomes with different treatment regimes, although statistically significant differences cannot be demonstrated due to low numbers of women using regimes other than LMWH throughout pregnancy (Table 4) causing limited study power.

LMWH throughout pregnancy was utilised by 71% of women and appears to be the preferred treatment in the UK. Despite doubts having been expressed about its efficacy in preventing maternal complications, it is neither teratogenic nor fetotoxic and therefore may be chosen by women prioritising the health of their baby. Although some previous studies report on a larger number of women with prosthetic valves in pregnancy<sup>1,15,20</sup>, our study includes the largest number of women with prosthetic valves managed with LMWH throughout pregnancy.

By 10 weeks gestation, 83% of women needed doses of LMWH higher than recommended in the British National Formulary<sup>9</sup>. Further dose escalation was needed between 10 and 20 weeks gestation. Cases of valve thrombosis associated with subtherapeutic Anti Xa levels in early pregnancy have been described<sup>16,20</sup>. Our data suggest that more appropriate starting



doses would be 2.5mg/kg for enoxaparin, 250iu/kg for dalteparin and 250iu/kg for tinzaparin to ensure minimal delay in reaching the target range.

Thrombotic complications were associated with a greater need for dose changes following monitoring of Anti Xa levels. Several authors have described thrombotic complications being more likely in association with subtherapeutic Anti Xa levels, either due to non-compliance or subtherapeutic dosing<sup>6,16,22,23,24,25,26</sup>. Although the importance of pre dose (trough) Anti Xa levels has been emphasised by some authors<sup>27,28</sup>, monitoring of trough Anti Xa levels has not been incorporated into specialist society guidelines<sup>7,29,30</sup>. There is a lack of consistency within the guidelines on frequency of monitoring, target ranges and the timing of post dose (peak) anti Xa levels<sup>7,29,30</sup>. It is therefore unsurprising that there was marked variation in the monitoring of LMWH treatment in our study. Outcomes may appear to be better in the women treated with warfarin, but this may be due to there being more consistent guidance regarding its monitoring and target ranges for MPHVs.

## **Conclusion**

This prospective national study reflects current UK practice since it included all women with a MPHVS, irrespective of gestation. It has shown that this rare condition is associated with a high risk of poor fetal and maternal outcome. Despite a lack of evidence to guide practice, the majority of women with prosthetic valves in the UK are using LMWH throughout pregnancy. There is wide variation in dosing and monitoring regimes, and the recommended weight based starting doses appear to be insufficient. The poor outcomes found in this group of women may relate to adequacy of their anticoagulation or may relate to the efficacy of LMWH itself. The information from this study may lead women and clinicians to re-evaluate this choice.

Women with MPHVS, and their clinicians need to appreciate the significant risks involved in pregnancy and need for specialist care to concentrate experience of this rare condition.



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383 **Contribution to authorship**

384 SV conceived the study, obtained funding, performed the analysis of the data and wrote the first  
385 draft of the manuscript. BC, CLT and CRMH contributed to the design of the study, and  
386 contributed to writing of the manuscript. MN designed the overall data collection methodology,  
387 supported the development of the study and contributed to writing of the manuscript.

388 **Details of Ethics Approval**

389 The UKOSS general methodology (04/MRE02/45) was approved by the London Multicentre  
390 Research Ethics Committee. This study was approved by the NRES Committee Yorkshire &  
391 Humber - Sheffield (study reference 13/YH/0048 – 7<sup>th</sup> February 2013).

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394 **Table Caption List**

395 Table 1 Demographic characteristics

396 Table 2 Haematological management during pregnancy and around the time of delivery

397 Table 3 Pregnancy outcome

398 Table 4 Overall maternal and fetal outcomes related to anticoagulation regime in pregnancy

399 (and expressed as a percentage of the number of women using each regime)

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Table 1 Demographic characteristics

<b>Characteristic</b>	<b>Number (%) of women (n=58)</b>
<b>Maternal age (years)</b>	
Median	31
Range	18-47
<b>Ethnicity</b>	
White British	38 (66)
Black British	2 (3)
African	7 (12)
Asian	7 (12)
Other	4 (7)
<b>BMI (kg/m<sup>2</sup>)</b>	
<20	13 (22)
20-24.9	22 (38)
25-29.9	14 (24)
30-34.9	3 (5)
>=35	5 (9)
Not known	1 (2)
<b>Smoking status</b>	
Smoked during pregnancy	13 (22)
Never smoked or ex-smokers	43 (74)
Not known	2 (3)
<b>Parity</b>	
Nulliparous	25 (43)
Parous	32 (55)
Not known	1 (2)
Range	1-5
<b>Reason for valve replacement</b>	
Congenital heart disease	29 (50)
Rheumatic heart disease	14 (24)
Endocarditis	9 (16)
Aortopathy	3 (5)
Not known	3 (5)
<b>Location of prosthetic valve*</b>	
Mitral	31 (53)
Systemic atrioventricular valve	1 (2)
Aortic	30 (52)
<b>Anticoagulation prior to pregnancy</b>	
Warfarin	49 (84)
Low molecular weight heparin	4 (7)
Dabigatran	1 (2)
No anticoagulation**	4 (7)

\*4 women had two prosthetic valves

\*\*3 non compliance and 1 woman had valve inserted during pregnancy

Table 2 Haematological management during pregnancy and around the time of delivery

<b>Anticoagulation</b>	<b>Number (%) of women who had presented and had ongoing pregnancies</b>		
<b>Overall regime for pregnancy</b>	<b>n=58</b>		
Warfarin throughout	3	(5)	
LMWH throughout	41	(71)	
LMWH in first trimester, warfarin till early 3 <sup>rd</sup> trimester then heparin prior to delivery	9	(16)	
Other	5	(9)	
<b>Anticoagulation at 10 weeks gestation</b>	<b>n=43</b>		
Warfarin	2	(5)	
Dabigatran	1	(2)	
LMWH	40	(93)	
Enoxaparin*	16		
Median dose(mg/kg)		2.2	
Dose range (mg/kg)		1.3-3.6	
Dalteparin*	4		
Median dose(iu/kg)		195	
Dose range (iu/kg)		187-321	
Tinzaparin*	10		
Median dose(iu/kg)		217	
Dose range (iu/kg)		133-405	
LMWH dose or preparation not known	10		
<b>Anticoagulation at 20 weeks gestation</b>	<b>n=47</b>		
Warfarin	11	(23)	
Other	3	(6)	
LMWH	33	(70)	
Enoxaparin*	15		
Median dose(mg/kg)		2.6	
Dose range (mg/kg)		1.3-4.2	
Dalteparin*	4		
Median dose(iu/kg)		341	
Dose range (iu/kg)		229-401	
Tinzaparin*	9		
Median dose(iu/kg)		337	
Dose range (iu/kg)		170-493	
LMWH dose or preparation not known	5		
<b>Anticoagulation around the time of delivery (&gt;24 weeks)</b>	<b>n=47</b>		
Converted to unfractionated heparin prior to delivery	11	(23)	
No change in dose or frequency of anticoagulation	4	(9)	
LMWH stopped during labour / prior to LSCS	19	(40)	
LMWH given but with a reduced dose, a dose omitted or given with a reduced frequency	7	(15)	
Other	3	(6)	
Not stated	3	(6)	

\*BNF recommended dose – Enoxaparin 1.5mg/kg; Dalteparin 200iu/kg; Tinzaparin 175iu/kg

Table 3 Pregnancy outcome

<b>Outcome</b>	<b>Number (%) of women</b>
<b>Pregnancy outcome</b>	<b>n=58</b>
Termination of pregnancy	4 (7)
Miscarriage	5 (9)
Maternal death with fetus undelivered	2 (3)
Stillbirth	1 (2)
Livebirth	45 (78)
Neonatal death	0 (0)
Not known	1 (2)
<b>Maternal outcome</b>	<b>n=58</b>
Maternal death	5 (9)
Cerebrovascular Accident	1 (2)
Thrombosed valve/ dysfunction	4 (7)
Serious maternal morbidity*	24 (41)
Cerebrovascular Accident	4 (7)
Thrombosed valve	5 (9)
Primary Postpartum Haemorrhage	1 (2)
Secondary Postpartum Haemorrhage	6 (10)
Wound haematoma	6 (10)
Intra-abdominal bleed	4 (7)
Vaginal haematoma	1 (2)
<b>Mode of delivery</b>	<b>n=47 pregnancies &gt;24 weeks gestation</b>
Spontaneous vaginal delivery	18 (39)
Instrumental vaginal delivery	3 (6)
LSCS in labour	1 (2)
LSCS prior to labour	24 (51)
Not known	1 (2)
<b>Onset of labour</b>	<b>n=47 pregnancies &gt;24 weeks gestation</b>
Did not labour	24 (51)
Induced	17 (37)
Laboured spontaneously	5 (11)
Not known	1 (2)
<b>Anaesthesia for LSCS</b>	<b>n=25 women delivered by LSCS</b>
Regional	16 (64)
General	9 (36)
<b>Neonatal outcome for livebirths</b>	<b>n=45 liveborn babies</b>
<37 weeks gestation	11 (24)
Birthweight <10 <sup>th</sup> centile for sex and gestation	14 (31)
<7 at 5 mins	5 (11)
NICU admission	14 (31)

\*3 women experienced more than one serious morbidity

Table 4 Overall maternal and fetal outcomes related to anticoagulation regime in pregnancy (and expressed as a percentage of the number of women using each regime)

	Poor maternal outcome	Poor maternal outcome	Good maternal outcome	Good maternal outcome	Total number of women using each regime
	Poor fetal outcome	Good fetal outcome	Poor fetal outcome	Good fetal outcome	
Warfarin throughout pregnancy	1 (33%)	1 (33%)	1 (33%)	0	3
LMWH throughout pregnancy	10 (24%)	13 (32%)	10 (24%)	8 (20%)	41
LMWH 1 <sup>st</sup> trimester then Warfarin	2 (22%)	1 (11%)	1 (11%)	5 (56%)	9
Other	1 (20%)	0	1 (20%)	3 (60%)	5
Totals	14 (24%)	15 (26%)	13 (22%)	16 (28%)	58