**Maternal Medicine CSG Meeting Minutes**

**Friday 25th May 2012, RCOG, U5 Collegiate Room**

1. **Present:** Prof Lucilla Poston, Prof Peter Brocklehurst, Prof Andrew Shennan, Prof Fionnuala McAuliffe, Dr Anna David, Dr Shakila Thangaratinam, Dr Lucy Chappell, Dr David Williams, Dr Dharmintra Pasupathy. On telephone: Prof Louise Kenny, Dr Jenny Myers, Dr Jason Waugh.

**Apologies:** Ian Crocker, Marian Knight, Shiao Chan, Marie Smith , Louise Webster, Cath Williamson

1. **Minutes of meeting at BMFMS April 2012**

These were unanimously approved.

1. **Prof Louise Kenny. STRIDER:** A Randomized Controlled Trial Of Sildenafil Therapy In Dismal Prognosis Early-Onset Intrauterine Growth Restriction. Proforma circulated prior to meeting. RCT proposed, with planned prospective IPD meta-analysis with four other groups seeking funding. Mechanism of action discussed with option of exploring mechanism through EME application (would need PI based in UK) as alternative to clinical trial alone. NZ trial of sildenafil funded and due to start imminently, with mechanistic work planned in parallel. Pharmacokinetics discussed; data available from previous studies in pre-eclampsia.

*Action: If Wellbeing unsuccessful, LP to email Fetal Medicine CSG chair (and for forwarding to members) to look for UK-based PI to lead EME application.*

1. **Dr. Anna David. The EVERREST project** - EVERREST: Does vascular endothelial growth factor gene therapy safely improve outcome in severe early-onset fetal growth restriction? Proforma circulated prior to meeting and already taken to Fetal Medicine CSG.

Funded by European FP7 call (6 million euros). First-in-woman phase I/IIa safety/efficacy study, with recruitment of first woman in approx 3 years. Entry criteria: severe early onset growth restriction, requiring delivery of therapeutic into uterine artery via interventional radiology. Care of woman would be transferred to UCLH. Rationale for occluding uterine artery for 5 mins to deliver vector discussed. Protocol will be developed over next 2 years.

1. **Prof Andrew Shennan.** **PARROTT:** Placental growth factor in Assessment of women with suspected pre-eclampsia to Reduce maternal morbidity: Randomised cOntrolled Trial, with test performance data from PELICAN study available imminently. Primary outcome: maternal morbidity, with sufficient power to show equivalence in perinatal outcome. Revealed vs. concealed randomisation, with subsequent clinical management guided by NICE recommendations for hypertension in pregnancy. Stratification by centre is in protocol to reduce heterogeneity from clinician management. Thresholds for PlGF discussed. Treatment paradox an issue; PREP study has used clinician management sticker to explore rationale for clinicians’ actions. Sample size: superiority for maternal outcome and equivalence or non-inferiority outcome for perinatal safety. Consider DQ at 2 years for follow-up of children.
2. **Dr Lucy Chappell. PITCH update**. Application being considered for EME call, which will focus on efficacy and mechanism from UK. Option of continuing with international collaboration on UDCA vs. placebo trial even if EME funded trial would be smaller number of participants. All EME applications in maternal medicine should come to MM CSG.
3. **Prof. Fionnuala McAuliffe. PIPS trial** – an RCT of probiotics to prevent and treat glucose intolerance in pregnancy. Proforma circulated prior to meeting. RCT of probiotics for four weeks in a) obese women and b) GDM women for longer duration. Possibilities of assessing gut microbiota discussed. Women will be asked to not take probiotics outside of the trial. Discussed issue that in GDM, women randomised to probiotics may have lower blood glucose at 2 weeks (and therefore not need insulin) whilst those on placebo may still have higher blood glucose at 2 weeks, be started on insulin, and therefore have lower blood glucose at 4 weeks. This would potentially mask any real effect of probiotics in GDM women.
4. **Dr. Shakila Thangaratinam.** Meta analysis project of the i-WIP collaborative network. (Lifestyle interventions in pregnancy). Application to HTA and Wellbeing for funding (previous commissioned call for evidence synthesis). Data from recent BMJ paper on systematic review and meta-analysis presented. NICE recommendations for research: effect of IOM compliance with GWG on clinical outcomes; effects in obese women and other sub-groups. Primary outcome: maternal weight gain and composite of adverse maternal outcomes. Supported by GONET. Heterogeneity between interventions is an important consideration, including compliance with diet or other intervention.
5. **Prof. Lucilla Poston.** **Preliminary discussion on TEST:** a first trimester screening study/ RCT of aspirin in prevention of pre-eclampsia on behalf of Prof Zarko Alfirevic. HTA recommend a test with high sensitivity/ specificity needed to be clinically useful. Three-arm trial proposed: a) ANC as per usual NICE recommendations; b) 150mg aspirin in nullips; c) first trimester screening with 150mg aspirin for those who are ‘test-positive’. Choice of screening test unclear – potentially based on biomarkers with/ without uterine artery Doppler screening (the latter may be difficult to implement in some centres). Option of going out to tender for screening test within HTA call, which could reduce the risk to the HTA. Most data available from Fetal Medicine Foundation publications, but testing often not in pure population of low risk nullips. Sample size: based on 5.4% pre-eclampsia/ SGA requiring delivery by 37/40 with 20% reduction (by 1.1%): requires 30,000 nullips. Fetal safety needs to be assessed, especially at dose of 150mg. Acceptability of giving aspirin to all nulliparous women is contentious as it medicalises normal pregnancy and may not be acceptable to women, midwives, obstetricians etc. Option of randomisation of revealed vs. concealed screening test, with subsequent randomisation to treatment or no treatment (with aspirin).
6. **Prof. Lucilla Poston.** Preliminary discussions on HTA call for trial on planned delivery for pre-eclampsia between 34 – 37 weeks of gestation. Several groups interested including those from KCL, QMUL with further interest from UCL, Newcastle, Liverpool. Research committee at RCOG consider best option to go for one co-ordinated application to HTA rather than competitive applications. HTA have considered option of multiple CIs (partly because of academic recognition) but they say not possible. Strong case for collaborative application within a MFM network, with CI role for consecutive trials shared between those able to undertake it, particularly as sample size will need to very large and include many units across UK, and inevitable duplication of effort. Important to build capability across several major units rather than all trials being based in one unit.

*Action: LP to arrange telecon between all interested parties to seek consensus if possible*

1. **AOB: Role of CSGs in prioritising research.**  Peter Brocklehurst discussed need to identify priorities for research in maternal medicine via MM network. This could include feeding in to HTA vignettes and other research funders (NIHR, Wellbeing). Strength in undertaking this as a national process, with lay involvement. Priorities will also be informed by research priorities from NICE guidelines. Need to be produced by November 2012 for RCOG meeting. May be relatively small projects e.g. satisfaction with care in labour. Discussion over development of PROMs in pregnancy – minimal work ongoing. Need for obstetricians to be represented on HTA panels (Khalid Khan and Jim Thornton on responsive board). Meeting in September will include consideration of research priorities (together with review of EME applications).

*Action: LP to invite lay members to join group prior to September meeting*

1. **Date of next meeting: 27 Sept 2012 at RCOG**